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Botulinum Toxin for NON-Surgical Lateral Release in Subjects with Patellofemoral Pain

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BOTULINUM TOXIN FOR NON-SURGICAL LATERAL RELEASE IN SUBJECTS WITH PATELLOFEMORAL PAIN

A Thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in Biomedical Engineering at Virginia Commonwealth University.

BY

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List of Abbreviations

Ag/Cl - Silver Chloride
AKP - Anterior Knee Pain
BTX-A- Botulinum Toxin Type A
BW - Body Weight
EME - Electromechanical Efficiency
EMG - Electromyography
EMPS - Electrical Motor Point Stimulation
FDA - Food and Drug Administration
FIQ- - Functional Index Questionnaire
FFT Fast Fourier Transform
Hz - Hertz
ITB - Illiotibial Band
IRB - Institutional internal Review Board
LEFS - Lower Extremity Functional Scaling
MMG - Mechanomyography
MnF Median Frequency
MVC - Maximum Voluntary Contraction
PFJ - Patellofemoral Joint
PFP - Patellofemoral Pain
PFPS - Patellofemoral Pain Syndrome
ROM - Range of Motion
RKE - Rotational Kinetic Energy
RMS - Root-Mean-Square
SEMG - Surface Electromyography
VAS - Visual Analog Scale
VL - Vastus Lateralis
VLL - Vastus Lateralis Longus
VM - Vastus Medialis
VML - Vastus Medialis Longus
VMO - Vastus Medialis Oblique

Abstract

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By Laura Theresa Maple, MS

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Previous studies for treating Patellofemoral Pain Syndrome (PFPS) are controversial regarding the effectiveness in alleviating anterior knee pain (AKP). The muscular imbalance between the vastus medialis oblique/vastus lateralis (VMO/VL) may be the underlying mechanical issue causing PFPS. It is hypothesized that Botox™ can decrease the force production capability of the lateral musculature mechanically similar to surgery. Strengthening the VMO while using Botox treatment can alleviating the muscular imbalance that occurs with subjects with PFPS.

A double blind study, having all participants blinded and uninformed of the injection contents, was implemented to test this hypothesis testing three female subjects. Four knees were treated. One subject received the Botox treatment and serially a placebo injection in the other limb. Two other subjects received placebo injections. EMG was executed to evaluate functional testing and the performance of the injections during extension exercises. Electromyography (EMG) data were collected from the muscle groups while the subjects performed forceful knee extension activities on an isokinetic dynamometer. In addition, kinetic jump data and self-reports of pain and activity were collected. Data were collected four times during a 12-week period.

The subject who received Botox™ injections expressed a significant decrease in reported PFP and an increase in daily activities. Botox™ was safe and effective in eliminating anterior knee pain. The VMO and VL resulted in similar fatigue indices at the completion of the 12- week study. The VMO and VL both resisted fatigue during at week 12.

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Chapter 1: Introduction

A. Overview of Patellofemoral Pain syndrome

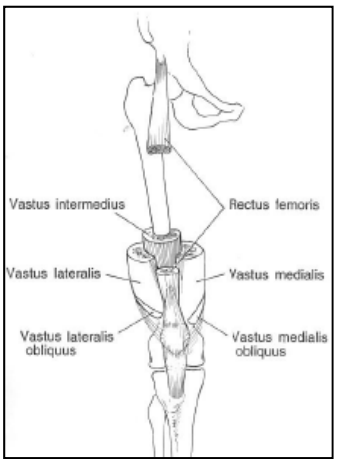
Patellofemoral pain syndrome (PFPS) is experienced by over 2.5 million Americans (Bentz, 2007) and is the leading cause of knee pain in patients under the age of 45. In addition, patellofemoral pain syndrome (PFPS) dominates knee ailments in regards to overuse injuries. According to a two-year study completed in 2002 by the University of British Columbia, 46 percent of more than 2,000 runners experienced severe PFP (Scott, 2007). Although the etiology of PFP remains elusive, strengthening the associated musculature can be effective in reducing chronic and episodic exacerbations of pain at the patellofemoral joint (PFJ) (Bentz, 2007).

Patellofemoral Pain syndrome is a term commonly used to describe a musculoskeletal condition that is characterized by anterior knee pain (AKP) (Ng, 2002). The pain is typically insidious in onset and affects the PFJ. The PFJ is defined as the articulation of the patella with the femoral condyles of the femur. The patella is part of a joint complex that includes the tibiofemoral joint and the tibiofubular joint (Ng, 2002). It provides a mobile yet firm site for ligaments and tendons to attach on the anterior side of the knee. The patella acts as an anatomical pulley and provides improved mechanical advantage to the tibiofemoral joint by increasing the ability of the quadriceps muscles to produce extension torque. The health of the quadriceps muscle complex is important for proper function of the patellofemoral joint.

The quadriceps muscle complex consists of the rectus femoris, the vastus lateralis (VL), vastus intermedius, and vastus medialis (VM). The locations of the muscles of interest and the patella are illustrated in figure 1.

Figure 1: Right Leg Illustrations for Key Points of Interest

A



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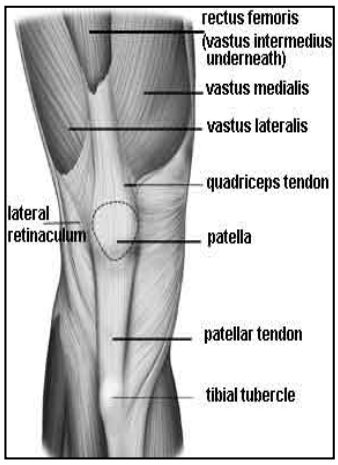


Figure 1: A. The figure above represents the four muscle groups of the quadriceps complex. B. Anterior view of the right leg illustrating the location of the muscle groups and tendon within the patellofemoral joint.

The rectus femoris muscle is the most superficial muscle of the quadriceps muscle complex. The vastus intermedius muscle is under the rectus femoris muscle and lies between the lateralis and medialis muscles. The VL lies lateral to the body of the femur (Ng, 2002), while the VM fibers are positioned medially from the longitudinal axis of the femur. The VM can be subdivided into the vastus medialis longus (VML) and the vastus medialis oblique (VMO) based on their fiber orientation. The VML is oriented more vertically similarly with the other rectus femoral fibers, whereas, the VMO is obliquely oriented at 55° off the longitudinal axis of the femur, thus distinguishing the muscle group from the other vasti muscles (Farahmand, 1998).

The fiber orientation of the VML make it better suited to contribute to knee extension torque. The VMO fiber orientation allows it to play a role in stabilizing the patella during extension activities. However in subjects with PFPS, the VMO may be proximally positioned and abnormally oriented. When the VMO muscles pull vertically in their line of action with the other rectus femoris muscles the oblique line of pull is reduced. Unlike its vertical oriented counterparts, the VM is considered to be the weakest and most vulnerable muscle to atrophy of the extensor mechanism because it is the only quadriceps muscle to have an oblique line of pull; the position can be affected causing PFPS (Sanchis-Alfonso, 2006). This is a recognized as a contributing factor in PFP patients with abnormal patellar movement (Ng, 2002 & Vicente, 1993).

Soft tissue structures can also contribute to abnormal patellar movement. These are tissues include the iliotibial band (ITB). The ITB is a fibrous band whose origin is near the hip, proximal of the gluteus maximus and minimus muscles. As the band descends, it splits medially and laterally forming the IT tract. This tract blends with the VL muscle and contributes to lateral pull on the patella. Excessive lateral pull on the patella can create exacerbate patellofemoral pain syndrome.

The etiology of PFPS has been reported to transpire with women more than men due to their anatomical pelvic structure (Sanchis-Alfonso, 2006). Women tend to have a wider pelvis. This can result in a greater lateral pull on the patella due to the resulting lower extremity geometry. It is believed that women suffer from PFPS more than men, in part, due to this geometric difference (Fredericson, 2006). The Q-angle is defined as the biomechanical Q-angle is defined as the angle between the line of pull from the patellar tendon to the anteriosuperior iliac spine and the resultant vector from the middle of the patella to the anterior tibial tuberosity

on the tibia (Fredericson, 2006). The line-of-pull of this muscle group creates an oblique pull that forms a laterally obtuse angle which is called the quadriceps, or Q, angle as shown in figure 2. The Q angle is normally small, approximately 10-15° in extension and is 0° in flexion when the femur rotates laterally with respect to the tibia (O'Brein, 2001). The reduction in Q-angle is associated with a valgus patellar force during quadriceps muscle contraction (Fox, 1993). The VMO vector forces can counteract the strong VL forces stabilizing the patellofemoral joint.

The patella relies on the balance of the quadriceps muscles and soft tissue structures to control medial and lateral tracking during the demands of daily activities. When patellar movement is compromised, normal activities can lead to shearing and compressive forces that may contribute to pain (Ng, 2006). Normal walking can produce compressive forces across the tibiofemoral joint exceeding five times body weight (BW) (O'Brien and Fox, DATES). For the same activity, forces at the PFJ are only about ½ x BW. However, other common daily activities increase PFJ forces significantly. Examples include: (1) ascending stairs → PFJ forces equal 1½ x BW, (2) descending stairs → PFJ forces equal 3 x BW, (3) squatting → PFJ forces equal 7.6 x BW, and (4) jumping → PFJ forces can exceed 20 x BW (Ng, 2002). Inappropriate alignment of the patella during these activities can strongly influence pain symptoms. Other factors that reported to contribute to PFP include: tight gastroconemius and quadriceps muscles, delayed VMO activation, hypermobility of the patella, and decreased power of the quadriceps muscles (Ng, 2002).

Patellofemoral misalignment and poor patellar tracking have been correlated with PFPS. Forces produced by the VL muscle may cause lateral patellar tracking and increase compressive forces under the lateral patellar facet. This weight-bearing facet is already under greater contact pressure than the medial facet (REF). The line-of-pull of the VMO muscle tends to counter this

affect. Any mechanical relationships or activation of these muscles can produce alteration of the tracking that may increase pain (Grelsamer & McConnell, 1998 and Ng, 2002).

B. Current Treatment Options for PFPS

There are several ways currently employed in the treatment of PFPS. One rehabilitation program incorporates taping techniques to improve patellar tracking. In this technique, Kinesiotape™ (an elastic tape) is applied over the patella to pull it in a medial direction. It is thought that this temporarily relieves the PFP if the pain was caused by maltracking and the associated increase lateral patellar pressure. This allows the patient to strengthen the medial muscles, stretch lateral structures, and restore balance to the system (McConnell, 1986). When muscle balance is restored, it is hoped that the tape is no longer necessary. The McConnell patellar taping program is intended to correct patellar tracking by medializing the patella.

The McConnell taping method (Grelsamer and McConnell, 1998) and physical therapy (rest, ice, or combination) are the often the first measures taken to reduce PFP. Another method of treatment is muscle stimulation. In this technique, medial muscle groups are electrically stimulated at a low frequency. The treatment is done daily for up to 8 weeks in hopes of improving the force production characteristics of the VM muscle. This treatment method has been reported to have some positive outcomes (Kannus, 1999).

A surgical method of treating PFPS is termed a lateral release. In this procedure, lateral retinaculum of the patella is cut to reduce the lateral forces produced by this fibrous tissue (Fox, 1993). Following recovery, it is hoped that the patella will track in a more normal fashion thus reducing PFP.

All of the aforementioned treatment methods for PFPS have one thing in common; they are all attempting to correct a mechanical imbalance in forces surrounding the patella that are thought to contribute to the patient's reports of pain. Reducing pain is ideal in any rehabilitation program since it allows normal movement patterns to be restored (Fox, 1993 and Fredericson, 2006). Each method has had limited success, but no one method has shown long term improvement with all patients. A new method of treatment is being proposed in this study to rebalance the muscle surrounding the patella by temporarily decreasing the force production capability of the lateral muscle group. It is hoped that this will decrease pain and increase the exercise tolerance of the patient so that force production balance can be restored.

C. The Nature, History, and Usefulness of Botulinum Toxin Type A

Botulinum Toxin Type A, (BTX-A), is more commonly known as Botox™ (Botox™, Allergan, Irvine, CA). Botox™ is a poison which acts at nerve endings and inhibits the release of acetylcholine, thus decreasing muscle force production. In controlled doses, the muscular paralysis is reversible and can ameliorate symptoms in patients with muscle imbalances (Tortora, 1996 & Sastre-Garriga, 2001). When used for PFPS, chemodenervation can persist for three months (Lim, 2006 and Singer, 2006). After this time, axonal branching is re-established with the neurotransmitter junction.

In 2006, Allergan Inc. reported Botox™ had helped patients get relief from certain medical conditions throughout 75 countries. Rajeev Nagi, a director of sales and marketing in India for Allergan Inc., claimed Botox™ had approximately 20,000 users in 2007 (Botoxcosmetic.com). Botox™ has been approved by the U.S. Food and Drug Administration (FDA) as a cosmetic treatment and to medically treat some dystonias (Sastre-Garriga, 2001). It

is reported safe, but does have some potential side effects. Users may experience local allergic reaction, hematomas, and burning at injection sites or anaphylactoid reaction caused by injections and excessive weakness that can persist for 3 to 6 months.

One of the problems with traditional therapies to improve the muscle balance surrounding the PFJ is that all of the quadriceps muscles have common neural innervations. As a result, it is nearly impossible to strengthen one quadriceps muscle without strengthening all of them (Barney, 1980). If isolated strengthening is required to restore overall balance in the system, then Botox™ can be used to selectively inhibit the VL muscle group. Subsequent exercise will strengthen the VMO muscle without activating the antagonistic VL muscle.

D. Supporting Studies

Research has previously reported using Botox™ injections to relieve PFPS. In 2006, Singer et al deemed the use of Botox™ as a potential treatment for AKP in an 8 female open labeled PFPS study. The purpose of this study was to reduce relative overall activity of the VL muscle while retraining the antagonist VM muscle with 12 weeks of physical therapy. Subjects reported reduced knee pain and increased participation in daily activities. Isometric quadriceps muscle strength was maintained or improved at the 24-week follow-up. This was regarded as a novel approach to improve patellofemoral mechanics to establish treatment efficacy.

Another opened labeled pilot study at Virginia Commonwealth University (VCU) investigated the use of Botox™ in a male subject with bilateral PFPS. The results showed improvement in power and torque generation at the knee. In addition, there was an increase in

VMO muscle fatigue resistance. Following the Botox™ injection, pain diminished at week seven and had not returned at a 67 week follow-up.

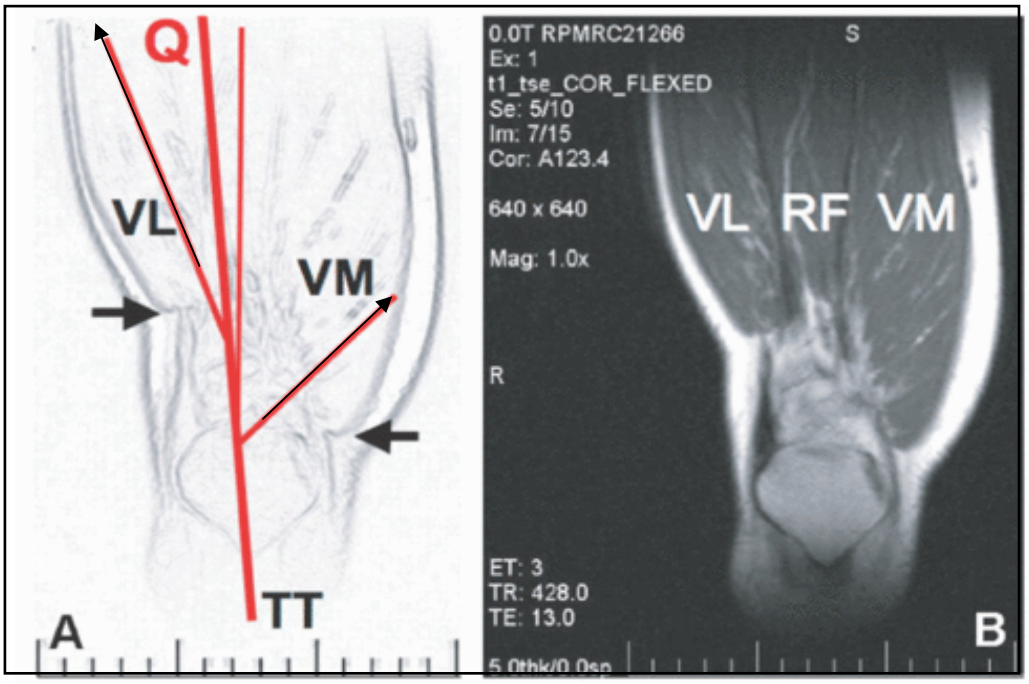
E. Rationale for Study

It's theorized that PFPS, is in part caused by VMO:VL muscle imbalance. While healthy knees are speculated to have a 1:1, VMO:VL EMG ratio, this ratio has been reported to be approximately 0.54 in PFP patients (Ng, 2006). A value of less than 1 implies that the VMO is producing less force that the VL. This altered ratio can negatively impact the biomechanics of the patellofemoral joint and contribute to improper patellar tracking. It is hypothesized that VMO muscle weakness results in an imbalance with the antagonist VL muscle, contributing to maltracking (Fredericson, 2006). The VL is the largest component of the quadriceps groupin subjects with PFPS (Faramond, 1998) and supplies the most power. It pulls the patella proximally then laterally during extension. If this force is not countered by the medial muscle group, then mechanical tracking problems can result. The maltracking may produce pain during knee extension.

Pain has a secondary effect of altering the activation timing of these muscles. In 2006, Sanchis-Alfonso reported changes in VM and VL activation in subjects with PFP during voluntary knee extension. The movements included both concentric and eccentric contractions. PFP subjects were compared to non-painful controls. The findings showed that during contractions, subjects with PFP had delayed VM activation. This would further compound the negative impact of muscle imbalance. The use of Botox may be able to address the valgus VL Q-angle associated with PFPS by strengthening VMO muscles. Stronger VMO muscles may

reduce patellar maltracking during extension and reduce knee pain. Figure 2 illustrates the Q-angle geometry within the PFJ along with the force vectors and insertion points for VL and VMO muscle groups. Subtle alterations in summative force development and action, due to the inhibitory effect of BTX-A in vastus lateralis [VL] and improved activation of vastus medialis [VM], may potentially contribute to reduction in joint symptoms (Singer, 2006).

Figure 2: Q-angle geometry. The figure represents the Q-angle within the PFJ. "Schematic depiction of the force vectors acting across the PFJ to the tibial tubercle (TT) [A]. Arrows show relative insertions into the quadriceps tendon, which are demonstrated in the frontal plane MRI in a normal individual [B] (Singer, 2006).



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Direction of pull is illustrated for the VL and VM muscle groups.

The largest problem in treating patients with mechanical PFPS is the inability to isolate the VMO muscle and to selectively increase its force production capability. If improper lateral patellar tracking is truly the cause of the PFP in these patients, then increasing the pull of the

VMO muscle to balance the VL muscle force would seem vital in restoring normal patellar movement. Past rehabilitation efforts have focused on identifying techniques to selectively strengthen the VMO to improve the force balance on the patella. To date, the current treatment options only provide temporarily relief and do not address the underlying biomechanical deficiencies of the PFJ.

F. Statement of Purpose

The purpose of this research study is to further test the effectiveness of Botox™ in the treatment of muscular imbalances related to PFPS. The study extends the impact of previous findings by employing a closed-label double-blind protocol. This minimizes the effects of examiner and subject bias on the results. Collected data will include kinematic, kinetic, and surface electromyography (sEMG) to analyze mechanical, spatial and temporal relationships of muscle that contribute to patellar movement. Additional self-report data will be collected from subjects to assess their perceived change in pain resulting from treatment. All data collection and utilized instrumentation were similar to unpublished pilot work.

Chapter 2: Experimental Methods

A. Subject Enrollment

The study was designed using a double blind protocol approved by the VCU internal review board (IRB). The IRB ensures human research conducted at the University is compliant with federal, state, and local regulations. The protocol was written with an expectation that 20 subjects would be recruited over a year time frame from a sample of convenience. Previous literature using preliminary data found Botox™ treatment as a novel approach to restoring knee extensor muscle balance with those with PFPS. Therefore all subjects were pre-screened by a licensed physician executing past literature criteria for PFPS. After pre-screening, the subjects could enroll in the study if they met the following inclusion criteria:

- 18-40 years of age
- anterior knee pain (AKP)
- pain during at least two of the following activities: climbing stairs, hopping, kneeling, prolonged sitting, running, and squatting
- the subject must have insidious onset
- patellar pain averaging at least 4 cm on a 10 cm visual analog scale
- knee pain for at least one month
- pain on patellar palpation

Subjects were excluded from the study if they had a history of knee surgery, dislocation, or clinical evidence based on history and clinical exam (See Appendix C form A).

Four female subjects met the inclusion criteria and were enrolled in the study. One of those subjects re-enrolled in the study after her other knee became symptomatic. She had already successfully completing the protocol on her first knee. Both knees met the inclusion criteria for this study and were treated serially. In total, 5 knees were treated. Subjects were randomly selected to receive either Botox™ treatment or placebo control. This random assignment resulted in one subject receiving Botox™ treatment. One subject decided not to continue after baseline testing and was removed from the study. The total number of knees treated in this study was n=4.

B. Target Data

Two types of data were collected in these experiments; subjective and objective. The *subjective data* included questionnaires designed to assess pain and functional levels. The *objective data* included quantifiable measures of performance.

Subjective Data

Subjective data is defined as data supplied by the subject. Questionnaires have successfully been used in anterior knee pain research to collect these data. These include the Anterior Knee Pain Scale (AKPS), Functional Index Questionnaire (FIQ), Lower Extremity Functional Scale (LEFS), and Visual Analog Scale (VAS) (Crossley, 2004 & Harrsion, 1995).

The AKPS is a 13-item questionnaire with discrete categories related to various levels of current knee function (Crossley, 2004). The subject is asked to rate their knee symptoms in regards to weight bearing support, presence of a compensatory limp, muscle atrophy, and pain when jumping, squatting, or running.

The FIQ questionnaire is an eight-activity multiple-choice rating form. Example FIQ questions include knee function when walking 32 blocks up to a mile. This toll is designed to assess functional abilities.

The LEFS rates exercises with a ratio scale of extreme difficulty to with no difficulty. The daily tasks that are rated include usual work, hobbies, bathing, walking, putting on shoes, squatting, lifting objects from the floor, performing light activities, getting in/out of car, walking 2 block to a mile, ascending/descending 10 stairs, standing and sitting for 1 hour, running on uneven ground, making sharp turns while running fast, hopping, and rolling out of bed.

The VAS can be used to quatify subjective data. In pain assessment, it is represented to the subject as a horizontal line, 10 centimeters in length, anchored by a pain descriptor at each end (see Appendix D). This descriptor is typically "no pain" at the left end, and "extreme pain" at the right end. The subject is asked to mark their perceived pain on the line with a vertical mark. The location of this vertical mark from the left end of the line is measured by the examiner. This allows the data to be converted to an ordinal scale for analysis.

Objective Data

Objective data is defined as data from physical exam or laboratory collection. Functional measurements such as, (1) jump height, (2) isokinetic force production, (3) isometric force production, and (4) fatigue measures are commonly used in exercise research to quantify subject performance.

1. Jump height

Force plates can be used to measure jump height. A force plate is an instrument designed to measure ground reaction forces in three directions; vertical, anterior-posterior, and medial-lateral. They are used in biophysics and human performance research. The plates are typically

mounted in the floor. When a force is applied to the plate, deformation is relative to the magnitude of the force applied. The deformation results in a proportional load cell voltage change (Grimshaw, 2006). If a subject is asked to jump vertically from a force plate and land back on the plate, their "hang-time" (or time in the air) is proportional to the height their center of mass was elevated. This *hang-time* can be converted to vertical jump height using the following constant acceleration equation:

$$\text{Jump height in inches} = 192\ (t/2)^2$$

All force plate data were sampled at 1000Hz with a 12-bit A/D converter and stored for off-line processing.

2. Isokinetic force production

Isokinetic testing is a reliable tool for strength assessments (Tiffreau, 2007), even in weak subjects. Isokinetic means constant velocity and requires a specialized piece of equipment called an isokinetic dynamometer. There are several available commercially and they are frequently used in rehabilitation and research settings. The isokinetic dynamometer is an electromechanical device designed to quantify extremity force production by having the subject perform against a constant velocity load through a defined range of motion. It is a dynamic test. A computer monitors force, angular velocity, and position of a rotating lever arm as the subject pushed against it. The maximum angular velocity is preset by the examiner. During isokinetic testing, the subject is instructed to push as hard as they can on the lever arm. As the preset velocity is reached, the dynamometer compensates by increasing the resistive load against the limb. This

limits the maximum velocity the subject can achieve and effectively creates an isokinetic environment. Force is recorded as the dependent variable and a measure of performance. Variable derivatives included average work, average power, and peak torque. In these experiments, the subject was set up to flex and extend their knee against the load.

The isokinetic testing protocol involved having the subject first perform a five-minute warm-up on a stationary bike at a 50 watts load (Coburn, 2005). The dynamometer (Biodex System 3, Biodex Medical Systems Inc, Shirley, NY) was setup for knee testing and adjusted to fit the subject based on the Biodex testing manual instructions (Figure 4). The Biodex is designed to control velocity and reliably measure power, angular velocity, and torque (Drouin, 2001). The subject was securely strapped in place in a seated position to minimize compensatory movements. Subjects were then asked to perform single limb concentric knee extension exercise at velocities of 180°/sec, 90°/sec, and 45°/sec through a range of 10°-90°. The range of motion (ROM) was set using a universal goniometer and standard anatomical landmarks (axis = lateral epicondyle, distal reference = lateral malleolus, proximal reference = greater trochanter). The lateral epicondyle was aligned with the axis of the Biodex moment arm to minimize shear force on the knee.

Figure 3: Biodex system

The subject was allowed to practice the isokinetic activity until they felt comfortable with the test. They were instructed to perform the knee extensions as quickly as possible and performed three sets of five repetitions. A 60-second rest was provided between sets. All isokinetic data were sampled at 1000Hz with a 12-bit A/D converter and stored for off-line processing.

3. Isometric force production

Isometric force production has been used to assess muscle function in previous research (Coburn, 2005). Isometric or static functional tests are used to evaluate muscular contractions at a fixed limb position. Theoretically, isometric contractions occur when the muscle develops tension with no changes in muscle length. In these experiments, force production was measured at 30°, 60°, and 90° of knee flexion. The Biodex was held in a fixed position and the subject was asked to forcefully extend their knee in a sustained contraction at each angle for five second. The force from this maximum voluntary contraction (MVC) was recorded. Three sets were performed at each angle with a 60-second rest between tests. All isometric data were sampled at 1000Hz with a 12-bit A/D converter and stored for off-line processing. The force data was converted to torque for analysis.

4. Fatigue measures

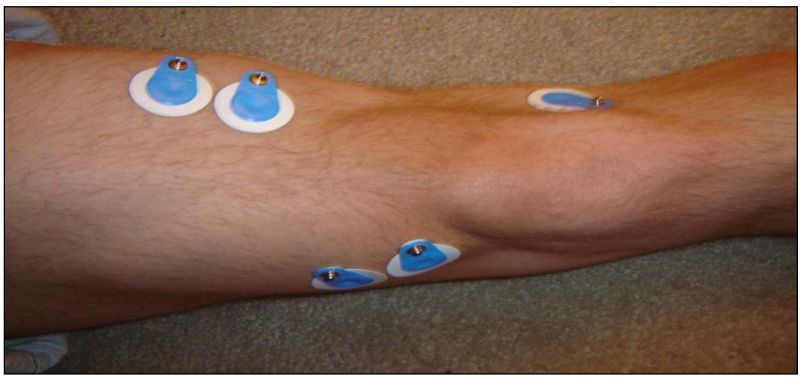
Fatigue is a reversible physiological phenomenon that can be measured during isometric muscle contractions (Ng, 2002). This is accomplished by recording the muscle's electrical

activity during the contraction. It can be done using surface electrodes with a technique called surface electromyogram (sEMG). The amplitude of the electrical activity is directly related to the muscle contraction force via the excitation-contraction coupling process. sEMG amplitude is often processed through a root-mean-squared (RMS) algorithm and has been shown to have a quasi-linear relationship with muscle force production (Kallenberg, 2008).

When submaximal isometric contractions are held until exhaustion, force production decreased. Findings suggest that a drop in mechanical efficiency contributes to this decline (Ebersole, 2008). Subsequent changes in the RMS signal can be observed (Wnek and Bowling, 2008). Changes in the power spectrum of the sEMG signal can be seen as well. The power spectrum is quantified by transforming time-domain data into the frequency-domain by employing a Fourier Transform. As a muscle fatigues, the median frequency has been shown to decrease (REF).

sEMG data collection was accomplished using a 4-channel commercial system (Noraxon Myosystem 1200, Scottsdale, AZ). This is a differential system with a CMRR of > 100dB and a bandwidth of 10Hz to 500Hz. Skin preparation involved cleaning the skin surface with 70% isopropyl alcohol and wiping it dry. Electrode pairs were place parallel to muscle fiber orientation for vastus medialis oblique (VMO) muscle and vastus lateralis (VL) muscle of the study leg using standard anatomical landmarks for reference (Figure 5). The VMO electrodes were placed superior and medial to the patellar apex a distance of “4-finger” widths. The VL electrodes were placed superior and lateral to the patellar apex a distance of “one hand-breadth”. The electrodes for each muscle group were approximately 2mm apart. A single ground electrode was placed on the lateral epicondyle.

Figure 4: Approximate EMG Placements for Vastus Lateralis and Vastus Medialis muscle belly and ground reference placements.



During the fatigue testing protocol, the subject was asked to sustain an isometric extension contraction at 80% of their maximum for 40-seconds with their knee held in a fixed position (60° flexion). Visual feedback provided a target to assist in this process. The 80% threshold was calculated by averaging the maximum isometric force data from the *isometric force production trials* performed at 60° of knee flexion. The fatigue test was repeated three times with a 60-second rest between trials. Verbal encouragement was provided. All sEMG data were sampled at 1000Hz with a 12-bit A/D converter. A digital 2nd order Butterworth filter was used to band limit the data between 20 and 200 Hz and the data were stored for off-line processing.

Fatigue was quantified by processing the sEMG data with a Fast Fourier Transform (FFT). The 40,000 data points (40-seconds at 1000Hz) were temporally processed in sequential windows of 1024 points with an overlap of 512 points. The median frequency (MnF) in each window was computed and stored. A time-indexed plot of these frequencies was created and a linear regression line was fit to the data. The slope of this line is an indication of relative fatigue with a negative slope indicating a fatiguing process (Yassierli, 2006).

C. Study Design

The study design included five treatment sessions. After the initial visit (session 0), data were collected four additional times over a 12-week period. Each subject followed the same outline and basic exercise regimen.

Session 0:

Documentation of subject medical history, physical exam (height, weight, blood pressure, and temperature), and a knee exam were performed. Data forms for inclusion, exclusion criteria, diagnosis, eligibility, subject name and contact information were collected. Subjective questionnaires on knee pain and function were given to the subject to document their knee pain three days prior their testing session.

Session 1: (3-7 days following session 0)

Baseline lower extremity functional and pain scale data were collected. The subjects were instructed to climb one flight of stairs and descend the same flight of stairs, rating their pain using the VAS. The subjects were also instructed to perform three independent vertical jumps on a force plate (Bertec model 4060). After completing the jump tests the subjects they rated their current anterior knee pain using the VAS. Isometric, isokinetic, and sEMG data were also collected.

Subjective data were collected by having the subject complete the AKPS, LEFS, and FIQ forms. In subsequent testing sessions, subjects completed this questionnaire at home, one day prior to arrival. The subjects were asked to record their data around the same time of day in an effort to improve the consistency of this measure.

Following the baseline testing, the subject was seen by study physician to receive injections of Botox™ or placebo. The pharmacy provided these materials in an unmarked syringe.

All examiners and subjects were blinded to the content of the syringe. The Botox™ dose contained 100 units of the drug. The placebo dose contained 1cc of saline, 1cc of 1% lidocane, and 1 drop of bicarbonate. The study physician administered the injections at four VL sites using ultrasound imaging to guide location. Finally, a physical therapist instructed the subject in the home exercise program (HEP) to be followed for the next 12 weeks. The details of this program can be found in the following section (D. Home Exercise Program).

Session 2-4: (Visits for 4, 6, and 12-week post injection)

Each of the next 3 sessions was the same. The subjects were asked to complete the pain scaling forms three days prior to the session. They were also asked to complete the AKPS, LEFS, and FIQ forms one day prior to the session. These forms were then returned to study director on the day of testing. At that time, subjects were asked if any changes in general health had occurred since last visit. Jump tests, stair-climb, isokinetic, isometric, and sEMG measures were taken and recorded as before. At the completion of the study, each subject commented on their overall improvement, consistency, or no change after treatment.

At the conclusion of each testing day the data were exported (Appendix B). Data analysis was performed with custom programs written with Matlab software (version 7.0; The Math works Inc., Natick, MA). Appendix C provides the calibration formulas to convert the Biodex data (voltages) into real-world values. Knee torque is defined as the Biodex load cell force x the length of the moment arm, where the moment arm length is the distance between joint center and the lateral malleolus of the subject.

D. Home Exercise Program

Subjects were provided with instructions for a home exercise program. These exercises were carefully selected since PFPS can be aggravated when patellofemoral compression forces are added to the joint. A description of each exercise their rationale follows.

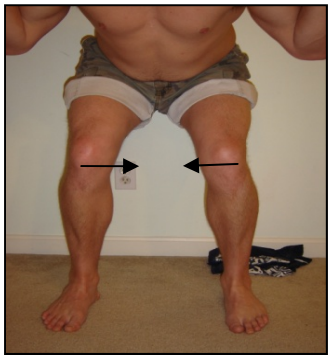
The HEP included:

- Single limb squats -- Squats isolate the VMO with medial adduction at the end of the squat. Performing single leg exercises ensures equal efforts per limb.
- Squats with hip adduction – The adduction exercises attempts to isolate the VMO.
- Side lying abduction -- The abductions exercise attempts to isolate the VL.
- Straight leg raises -- The straight leg raises strengthens the entire quadriceps complex as a whole maximizing quadriceps strength.
- Side raise hip adduction -- The adduction exercises attempts to isolate the VMO.
- Iliotibial (IT) band stretches -- IT band fibers blend and mix with the fibers of the lateral retinaculum, thus if they are tight, they can contribute to lateral patella tilting and excessive pressure on the patella. The IT stretches can allow the soft tissue of the patella tendon to loosen around the patella structure. It can also allow less lateral pull on the patella to occur with the knee, therefore, correcting or alleviating irregularities in patella alignment and possibly allowing relief. When a subject can increase the number of repetitions over load, the muscular endurance should increase while increasing VMO activity.

Figure 5: Exercise examples prescribed for subjects to complete daily.

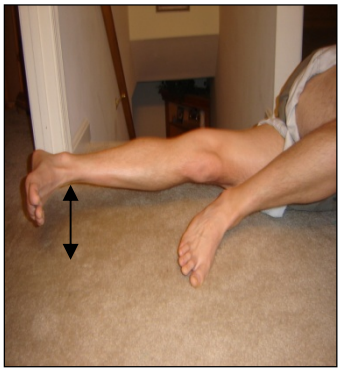
Single leg squats

Squats with adduction

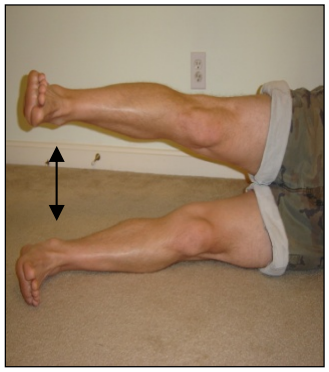


ITB stretches

Side lying adductions



Side lying abductions



Straight leg raises

The initial number of exercise repetitions and sets were titrated by a physical therapist according to each subject's reported pain. Each subject was asked to increase their exercises in repetitions or sets as they were able. Each subject kept a diary throughout the study to record and to track their progress. This diary was provided to the examiner at the conclusion of the study.

Chapter 3: Results

This study included the analysis of subjective and objective data. The subjective data included four subject questionnaires pertaining to pain and function. The objective data included kinetic, kinematic, EMG, and functional measures.

Over the course of two years, four subjects met the inclusion criteria and were enrolled in the study. Three completed the protocol successfully. One of those subjects re-enrolled in the study for treatment of her other knee one year after her initial testing. T his subject received the Botox™ treatment in one knee and the placebo in the other. Data from this subject is unique and allows a comparison of subjective results. Analysis of these data points will be labeled as a "Case Study". The total knees tested in this study was n=4. One additional subject is included in some of the presented results. These data are from a previous pilot study with a similar protocol in which the subject had both knees treated with Botox™.

Research bias was minimized by using a double blind protocol where subjects and researchers were blinded to the treatment type (Botox™ or placebo) during both the data collection and processing. Syringes were prepared by the MCV pharmacy and delivered to the physician unmarked. At the conclusion of the study, one subject had received the Botox™ treatment and three had received the placebo treatment. Throughout the remainder of this paper, subjects are labeled based on their injection type: Botox™, Placebo 1, Placebo 2, and Placebo 3. The case study data compares Botox™ to Placebo 2.

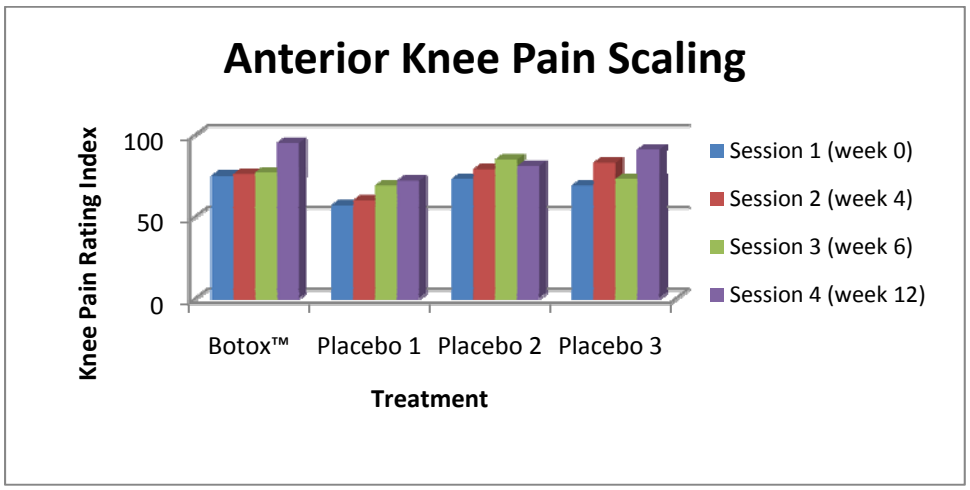
A. Subjective Results

Subjective data is defined as data supplied by the subject. The uses of subjective measures are well documented in the literature (Crossley, 2004). These were used to assess and quantify pain and functional changes throughout this study.

1. Anterior Knee Pain Scoring (AKPS)

The AKPS is a 13-item questionnaire with discrete categories related to various levels of current knee function (Crossley, 2004). The subject is asked to rate their knee symptoms in regards to weight bearing support, presence of a compensatory limp, muscle atrophy, and pain when jumping, squatting, or running. These questions are weighted and the subjects' responses are summed to provide an overall index. A score of zero implies severe disability; while one hundred represents no pain and normal function (Kujala, 1993). Figure 6 displays the subjects' AKPS results and compares subjects' progress internally and externally over the course of this study.

Figure 6: Anterior knee pain scoring for Botox™ treatment and placebo injections. This figure is a graphical representation of the data presented in Appendix A.

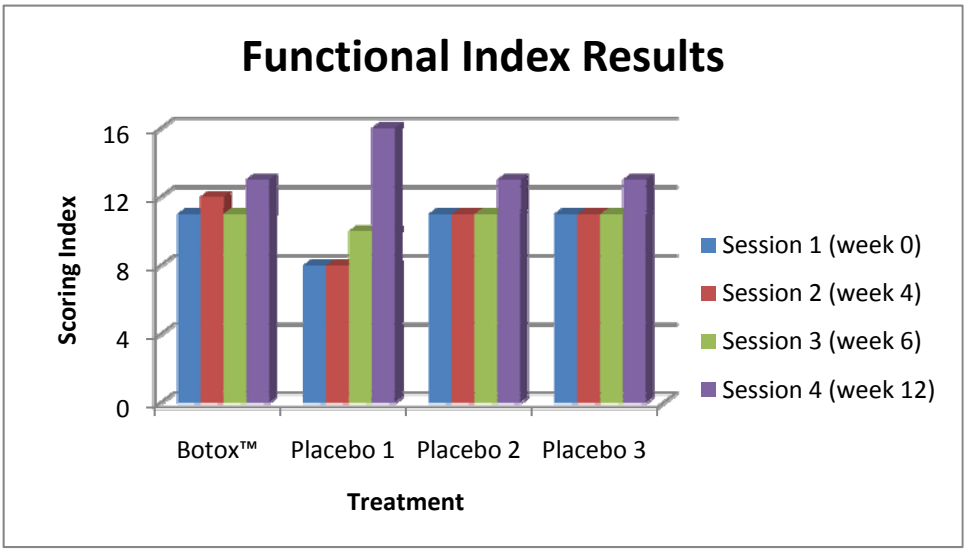


A positive change score represents an improvement in function and a decrease in reported pain. All subjects had a positive change score when comparing Session 1 to Session 4. The positive change score signifies sustainable improvement.

2. Functional Index Questionnaire (FIQ)

The FIQ questionnaire is an eight-activity multiple-choice rating form. The FIQ questions were weighted from zero to two based on the subjects' self-reported ability to complete specific tasks. The task scores were summed to create a composite score for each testing week. The highest achievable score was sixteen and the lowest was zero. A score of zero indicates the inability to perform all activities and sixteen indicates no issue performing any of the activities. Results are shown in figure 7.

Figure 7: Functional index scoring results for the Botox™ treatment and placebo subjects. This figure is a graphical representation of the data presented in Appendix A. A higher FIQ implies higher function capabilities.



All subjects reported an improvement in performing functional tasks when comparing Session 1 to Session 4.

3. Lower Extremity Functional Scaling (LEFS)

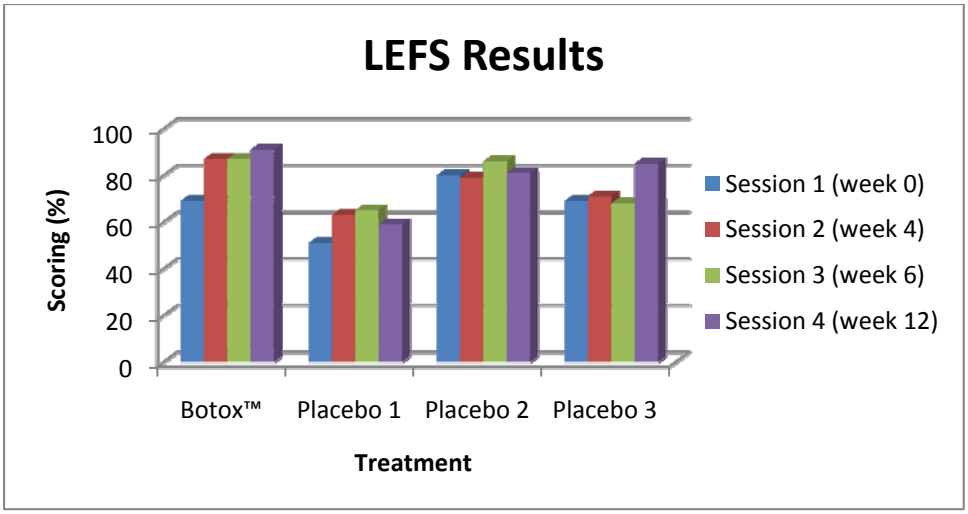
The LEFS is a 19-item questionnaire related to normal daily activities. The ability to perform these activities is objectively defined using the following criteria (Brinkley, 1999):

- 0 = the subject was unable to perform activity
- 1 = the subject had quite a bit of difficulty performing the activity
- 2 = the subject had moderate difficulty performing the activity
- 3 = the subject had a little bit of difficulty performing the activity
- 4 = the subject had no difficulty performing the activity

The sum of the scores was divided by the maximum possible points to create a percent composite score. The maximum obtainable score for LEFS is 76 points. A subject who experiences no difficulty with all 19 tasks would score a 100% as their LEFS result. Results are plotted in figure

8.

Figure 8A: Illustrates the LEFS results for the Botox™ treatment and placebo subjects. The Botox™ subject had a change score of +22%. The Placebo subjects had an average change score of +8%. This figure is a graphical representation of the data presented in Appendix A.

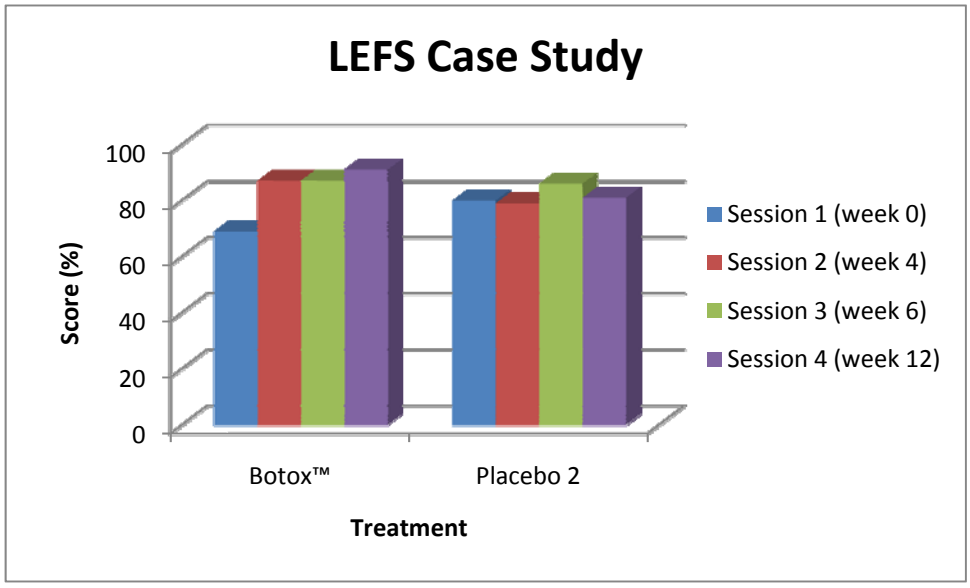


The subject treated with Botox™ had the highest overall score experiencing only mild difficulty performing squats, running on uneven turf, and making sharp turns while sprinting. All subjects were able to perform daily tasks, such as rolling in bed and getting in and out of the bath and vehicle. However, the placebo subjects reported extreme or mild difficulty with recreational activities, such as walking two blocks to a mile, squating, running on uneven turf, and making sharp turns while sprinting.

When comparing the Case Study results, the limb treated with Botox™ initally had a total score of 69%, but following treatment, progressed to 91% by week 12. The subject experienced little difficulty with 3 out of the 19 tasks. However, when the same subject later received the placebo treatment on the other leg (Placebo 2), the subject initally scored 80% and received a 12

week score of 81%, noting performance difficulty in 8 out of the 19 tasks. A comparision between the placebo control injective limb resuted in a higher rating of five points versus the Botox™ treated limb. These tasks included recreational activities, squatting, walking 2 blocks to a mile, sitting and standing for an hour, running on unven turf, and making sharp turns while sprinting.

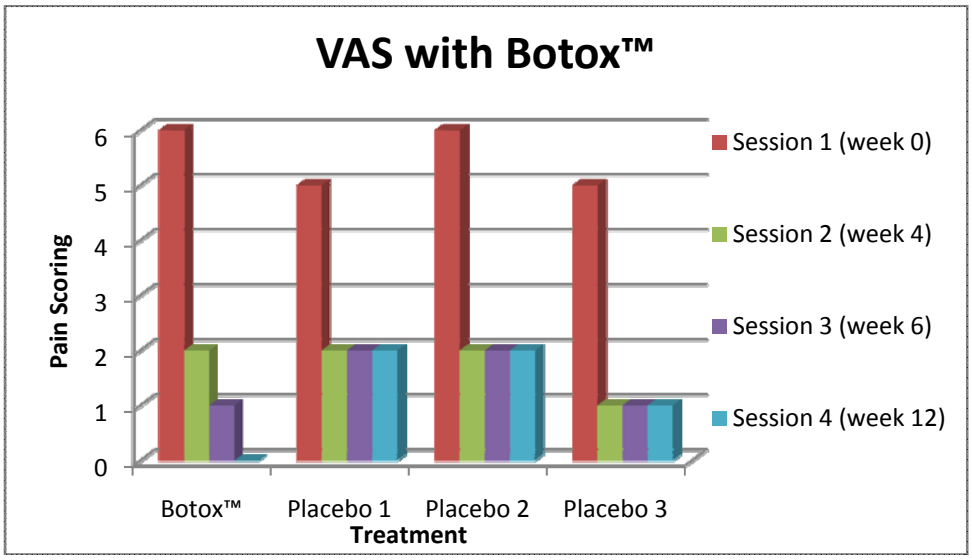
Figure 8B: Illustrates the LEFS results for the Case Study subject. The Botox™ subject had a change score of +22%. The Placebo2 had an average change score of +1%. This figure is a graphical representation of the data presented in Appendix A.

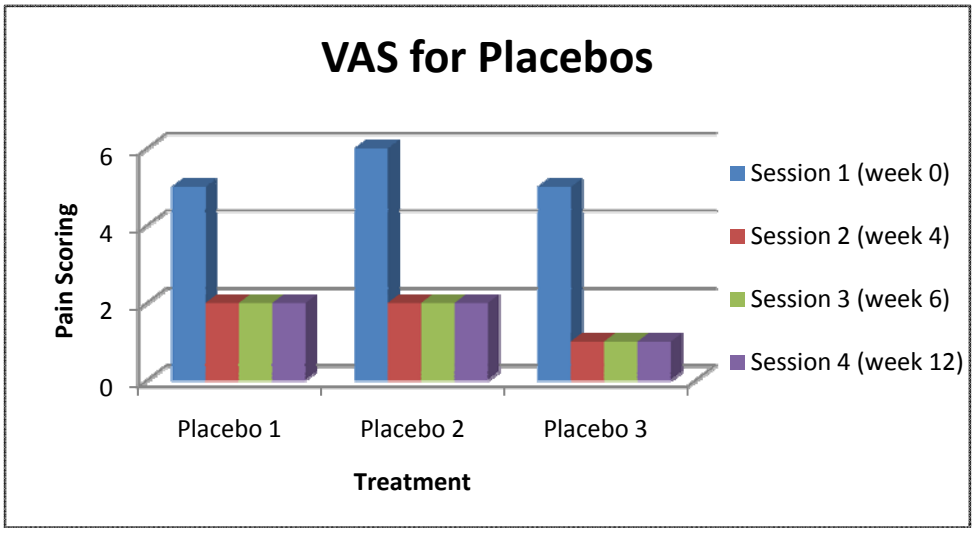


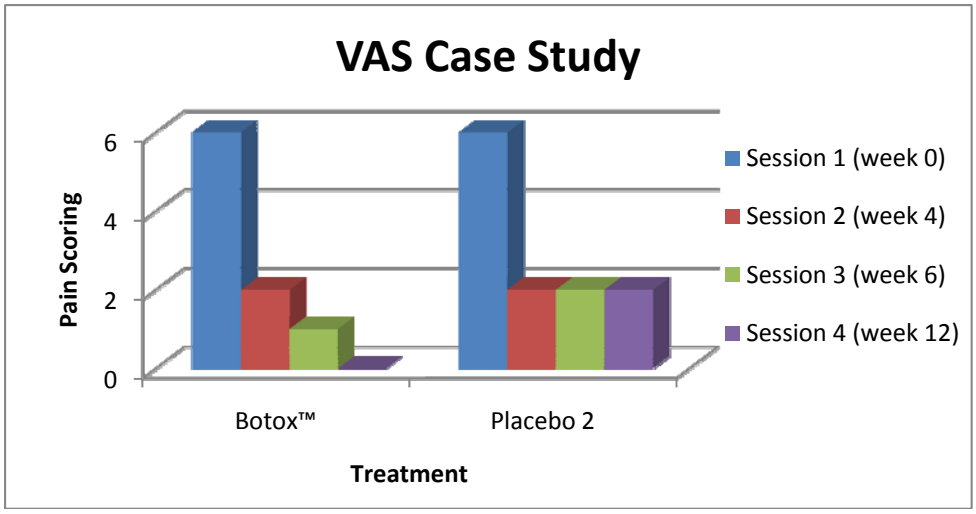
4. Visual Analog Scaling (VAS)

VAS is a measurement tool to assess knee pain characteristics that cannot be directly measured using other instruments (Gould, 2001). The amount of pain a subject feels ranges across a continuum from "no pain" to "extreme pain". The assessment is highly subjective and most valued when looking at change within subjects. These data are of less value for comparing across subjects (Gould, 2001). Figure 9 illustrates the VAS results for ascending and descending stairs and jumping for the subject treated with Botox™, averaged placebo, and case study data.

Figure 9: VAS Results for subject treated with Botox™.







The Botox™ subject perceived pain scoring diminished throughout the study for ascending and descending stairs and while jumping. Initially, pain was reported to be in the moderate to severe range. At the conclusion of the study, the subject reported no pain. The placebo controls continued to report mild pain at the end of the study.

C. Objective Results

Objective data is defined as data from physical exam or laboratory collection. Functional measurements were used to quantify subject performance. Testing was accomplished using an isokinetic dynamometer (Biodex), a surface EMG system (Myosystem 1200, Noraxon), and a force plate (Bertec). Data were again collected four times during the course of the study at weeks 1, 4, 6, and 12. Results are reported below.

1. Isokinetic Results

Concentric isokinetic leg extension data were collected using a Biodex isokinetic dynamometer (Biodex Inc, NY). Subjects were then asked to perform single limb concentric knee extension exercise at velocities of 180°/sec, 90°/sec, and 45°/sec through a range of 10°-90° of knee flexion. Intra subject data were averaged for each velocity. No verbal encouragement was provided during data collection to allow each subject to define their personal maximum effort. Work and power were calculated for each trial. The results are summarized in Appendix

a. Work

Work is defined by Newton's Second Law of angular motion. The law states that a net torque produces angular acceleration of a body that is directly proportional to the magnitude of the torque, in the same direction as the torque, and inversely proportional to the body's moment of inertia. This law is often stated as, "torque equals moment of inertia times angular acceleration ($T = I\alpha$)". Like its linear analog, the expression of for angular work is a function of force and distance moved:

W = T x θ
Where: T is torque in N-m and θ is the angular displacement in radians.
Work is measured in joules (J), which is defined as Nm or $kg \bullet m^2/s^2$.

When using the Biodex during knee extension activities, torque is produced by the subject when they apply a force to the rotating arm at some distance from the axis of rotation. Work is done when this torque produces angular movement of the arm. This can also be expressed as rotational kinetic energy ($RKE = \frac{1}{2} I\omega^2$; where I = the moment of inertia, and ω = the angular velocity in radians/sec). Figures 10A-D illustrate the angular work done in order of 180°/sec, 90°/sec, and 45°/sec using the work energy theorem. Average work, power, and standard deviations are presented in Appendix A9.

Figure 10A: Work results at 180°/s.

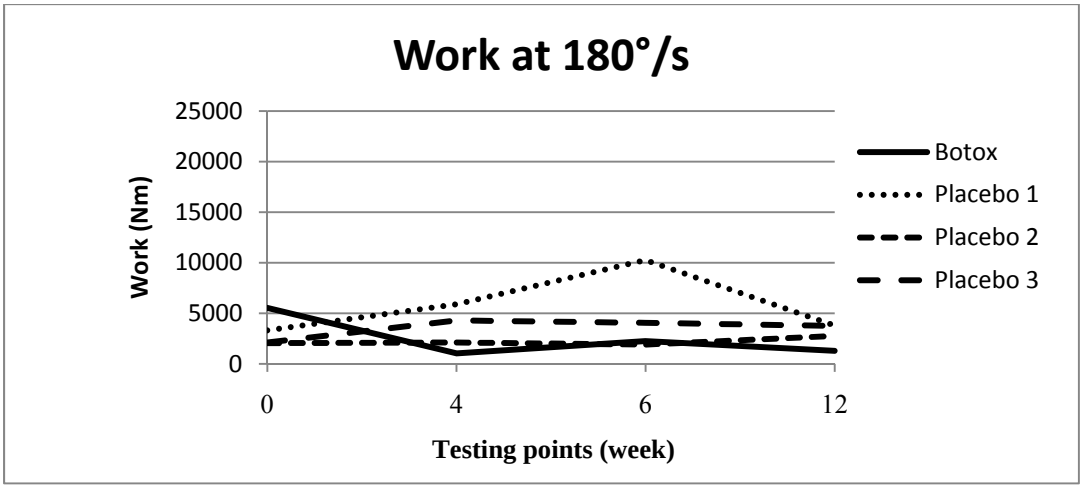


Figure 10B: Work results at 90°/s.

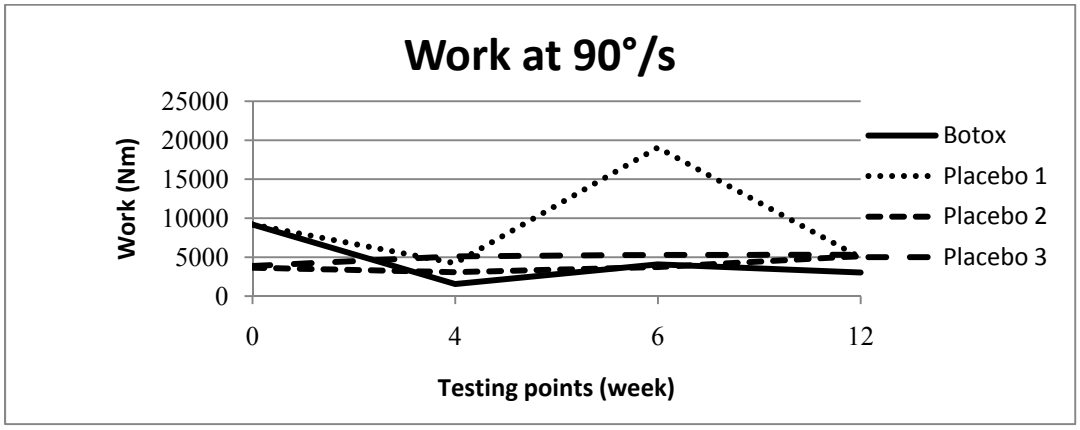


Figure 10C: Work results at 45°/s

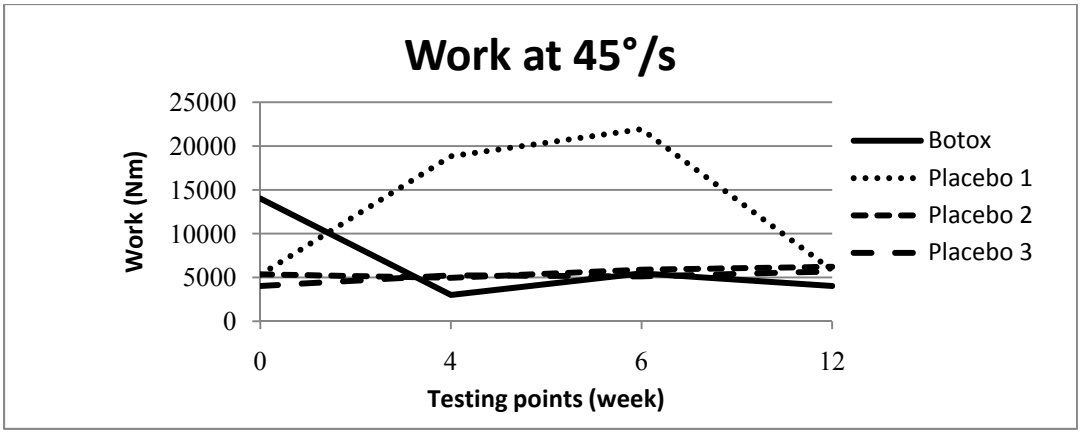
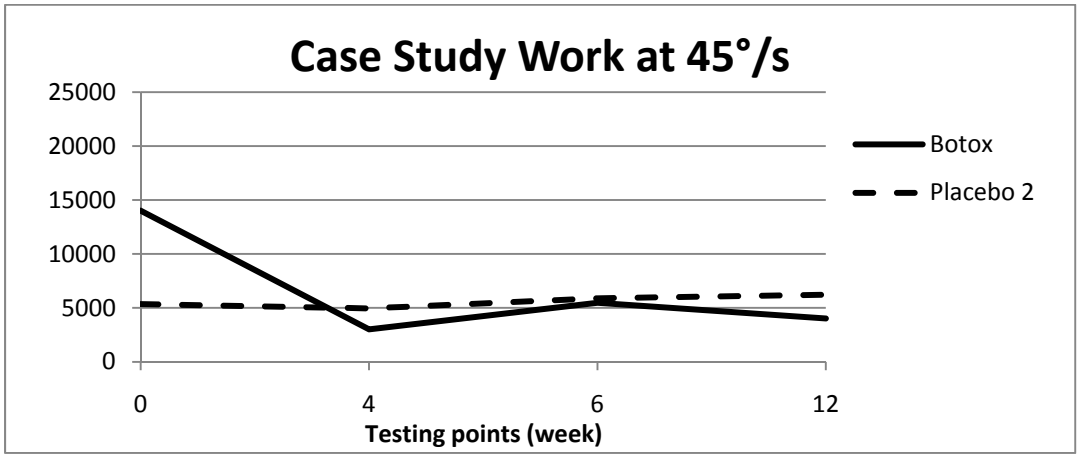


Figure 10D: Work results at 45°/s for Case Study



In general, angular work was greater at the lower angular velocities for all subjects. The Botox™ subject had a significant decline in angular work following the injection.

b. Power

Power is the product of torque and angular velocity. Power is defined as the amount of work performed per unit time (Cutnell and Johnson, 1997) and expressed at Nm/s (or Joules/s or Watts).

$P = T \times \omega$

Where: T is torque in N-m and ω is the angular velocity in radians/sec.

Figures 11A - D illustrate power results from kinetic angular motion testing at 180°/s, 90°/s, and 45°/s.

Figure 11A: Power results at 180°/s

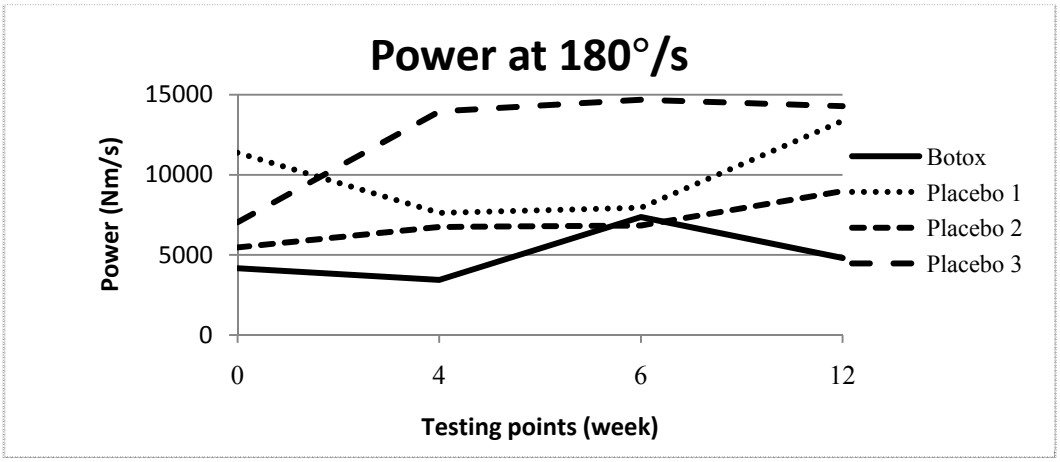


Figure 11B: Power results at 90°/s

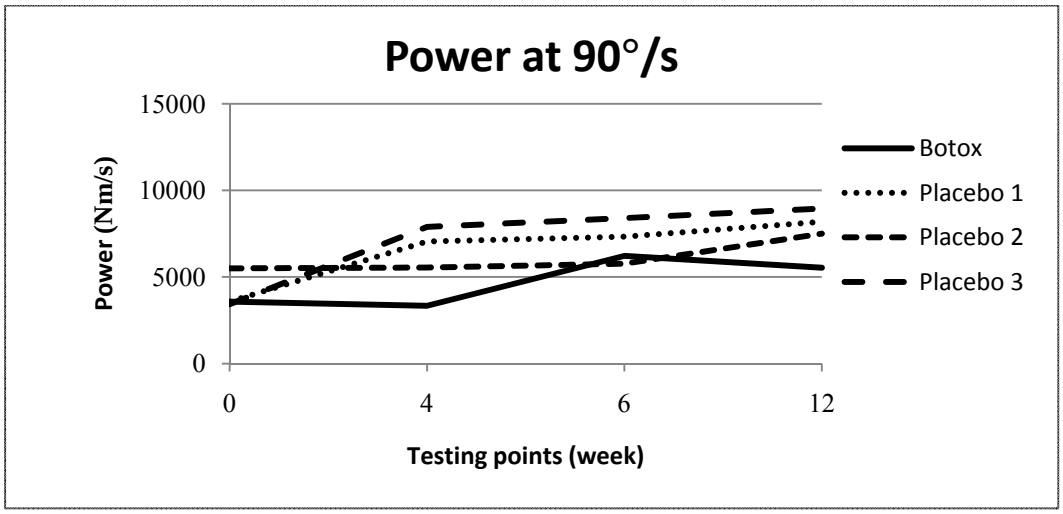


Figure 11C: Power results at 45°/s

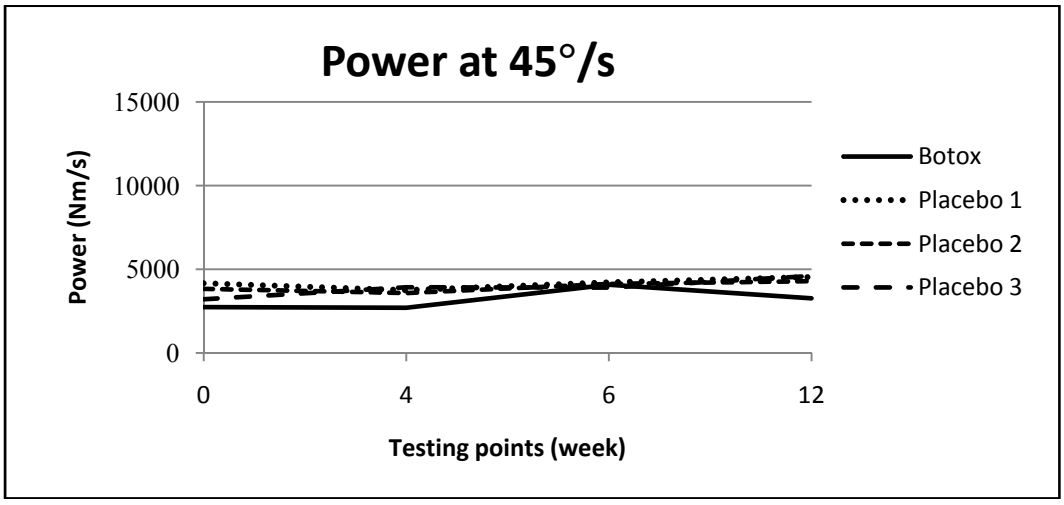
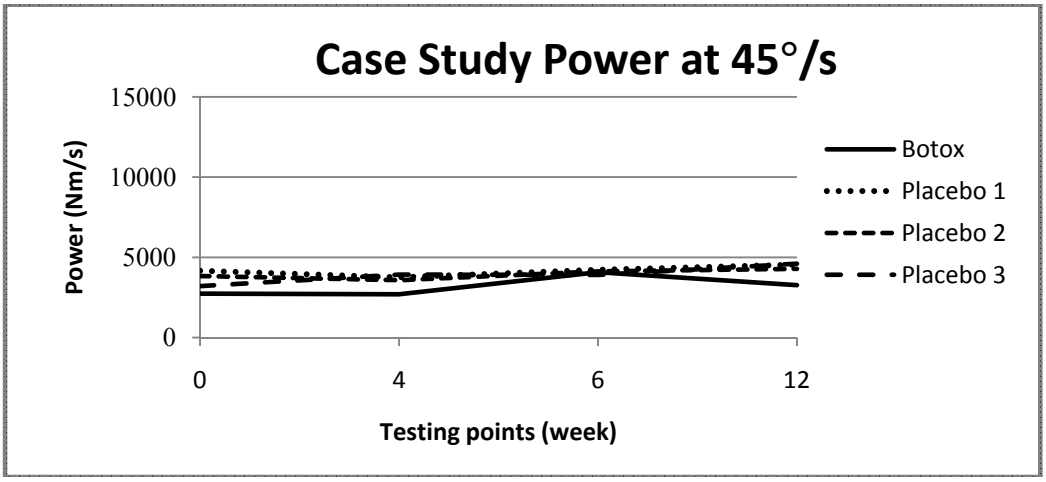


Figure 11D: Power results at 45°/s for Case Study



The power results illustrate more variability at the higher velocity with higher power generation at these velocities. The Botox™ treated subject was less powerful at week 4, but recovered by week 6.

2. Isometric Results

Using the Biodex to perform isometric contractions, torque was measured at prescribed angles. Torque is defined as:

Torque (τ) = $F\iota$ (Cutnell and Johnson, 1997)

Where: F is the magnitude of force and ι is the lever arm

Torque is measure in Newton * meter (Nm)

Isometric extension torque production was measured and recorded for orthopedic knee angles at 30°, 60°, and 90° of flexion. The isometric data for each subject was averaged for all trial sets. Results are plotted in figures 12A-C and the subjects averages are reported in appendix C.

Figure 12A: Botox™ subject torque results at 30. This figure is a graphical representation of the data presented in table 4.

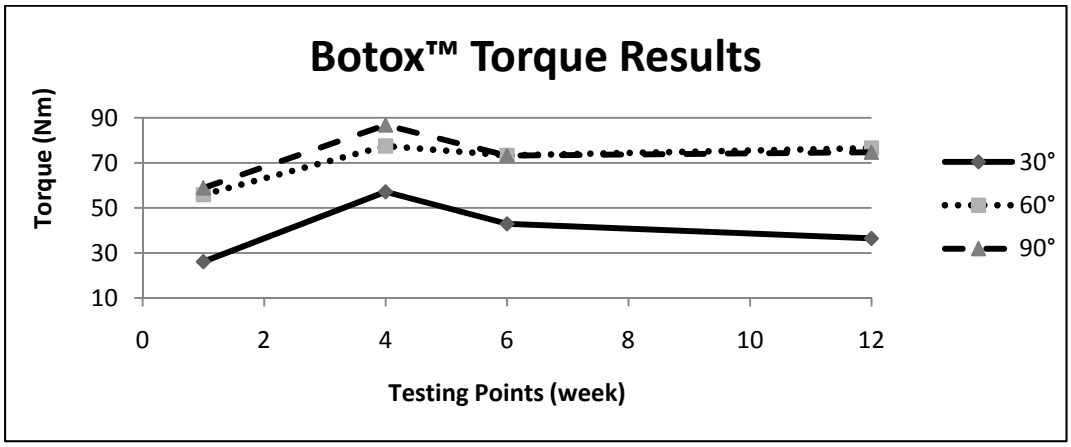


Figure 12B: Placebo torque results at all three isometric testing angles

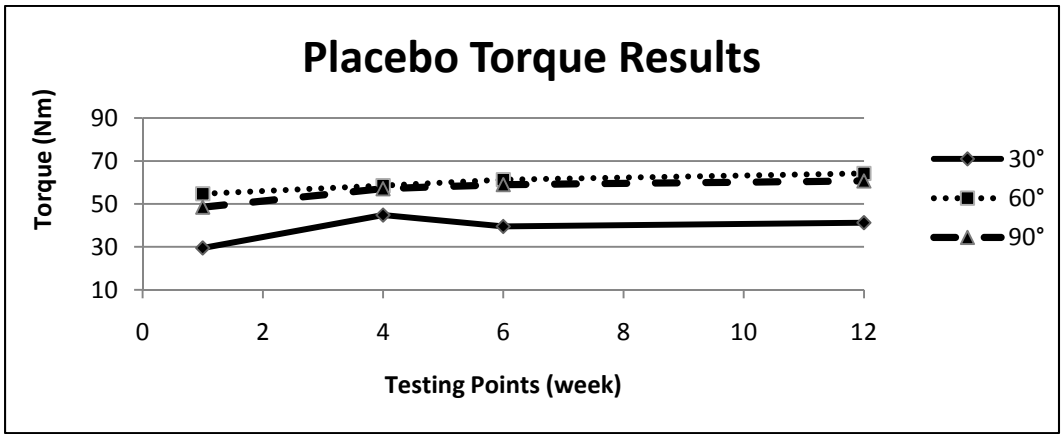
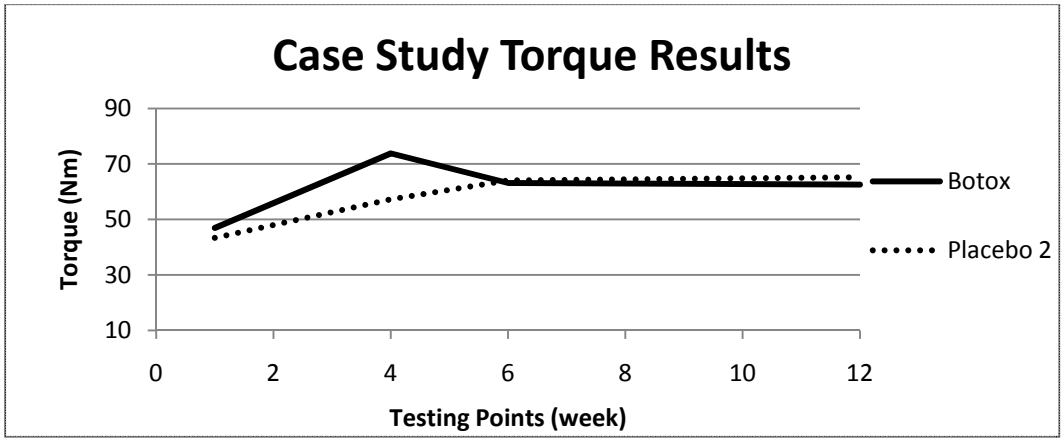


Figure 12C: Case Study torque results at 60°



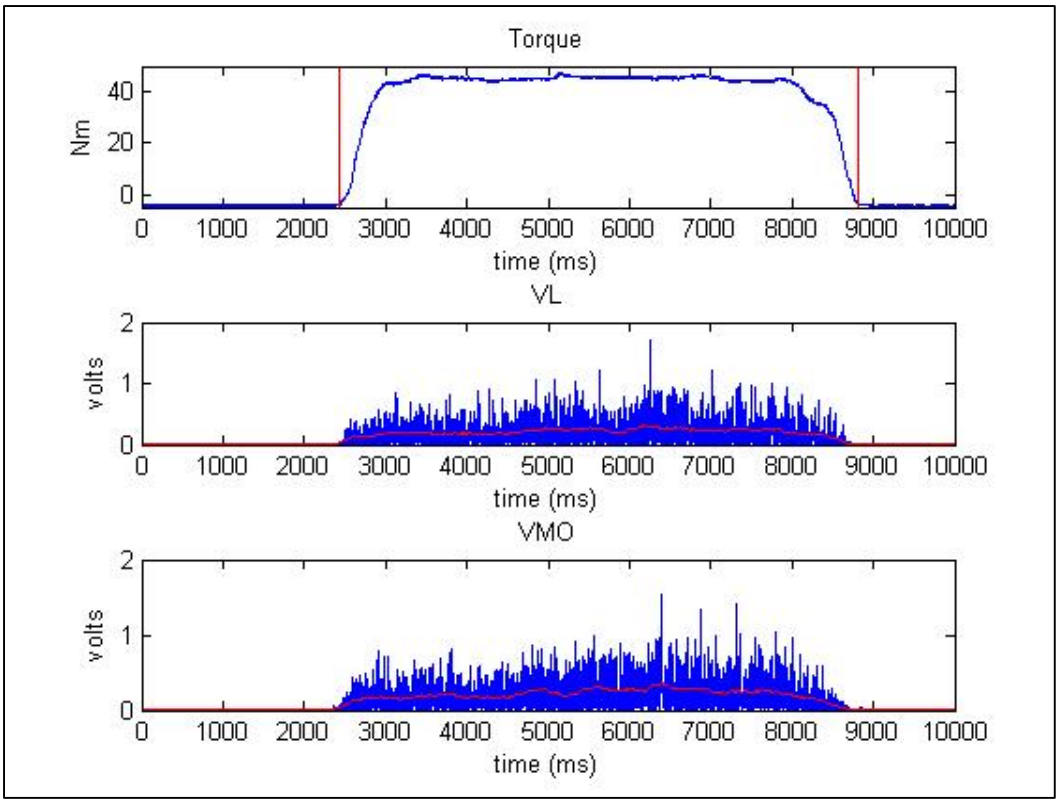
There is a similar pattern at all three isometric contraction angle. However, the ability to produce knee extension torque is maximized at a knee angle of 45° due to muscle length physiology and anatomical mechanical advantage, so it is expected that the torque levels at 30° and 60° would be greater than at 90°. Each subject increased their torque production over time with the highest amount of torque produced during the final week of testing.

Both the Botox™ and placebo limbs increased torque production at week 4, with the exception of placebo 3 in the 30° trail. The Botox™ treated limb produced the highest torque at 60°, but the placebo control 2 produced the highest overall torque.

3. EMG

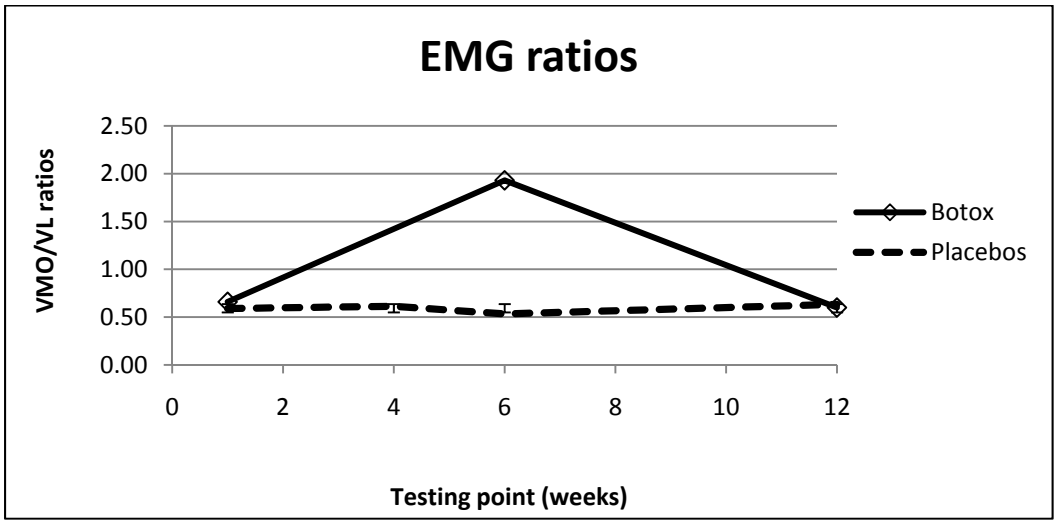
Electrodes were placed on each subject to measure VL and VMO muscle electrical activity during a sustained isometric contraction. The data was processed with a root-mean-square (RMS) algorithm to allow averaged magnitude data to be used to compute an activation ratio (VMO:VL). The RMS process involved full wave rectification of the EMG data, followed by digital integration using a 25ms time constant. Typical results are illustrated in figure 14A.

Figure 13A: The three plots in figure 13A illustrate typical sEMG responses during the isometric testing. Note that torque production was constaint during the contraction. Also note that the raw EMG data is presented in blue and the RMS data is presented in red.



In figure 14A, the top figure illustrates the production of knee torque initiated around 3 seconds and ending after 9 seconds. The middle plot illustrates typical sEMG results for the VL muscle. The bottom plot illustrates a typical sEMG response for the VMO muscle. From these data, EMG ratios were computed from the middle 3 seconds of contraction data. This was done by dividing the average RMS VMO value by the average RMS VL value. Isometric contractions were tested at 30°, 60°, and 90° of knee flexion. In figures 14A and B, VMO:VL EMG signal ratios are illustrated at 60°. These ratios were used to report relative muscle activity for all trials.

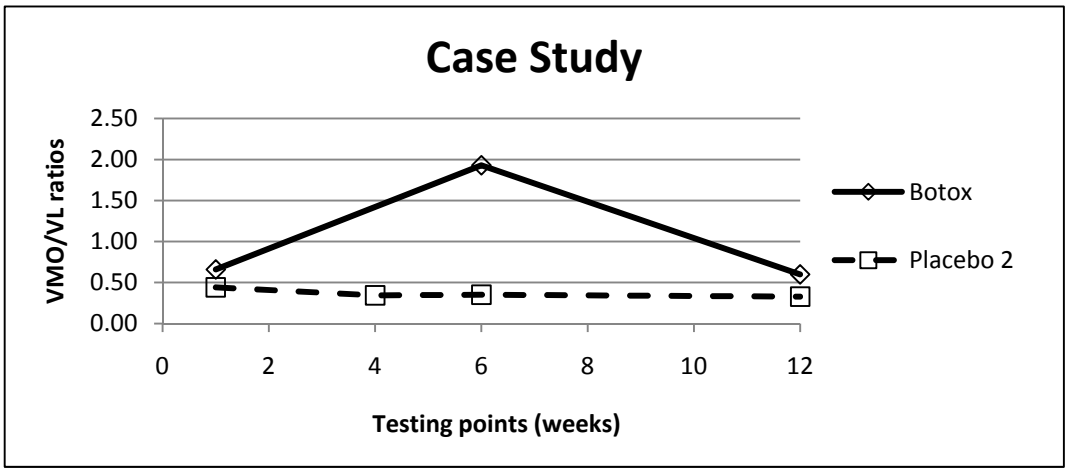
Figure 14A: VMO:VL EMG signal result ratio for Botox™ and the placebo controls averaged data at the 60 ° position.



SEM was 0.043 for VMO/VL for placebo control ratios. Small values signify that the means for each placebo differ by 0.043. This implies a consistency within the placebo data.

These data suggest that the VMO was more active that the VL muscle at week 6 in the Botox™ treated subject. This ratio returned to baseline by week 12. The average placebo data showed no change over the course of the treatment. Figure 14B illustrates a similar trend in the Case Study comparison.

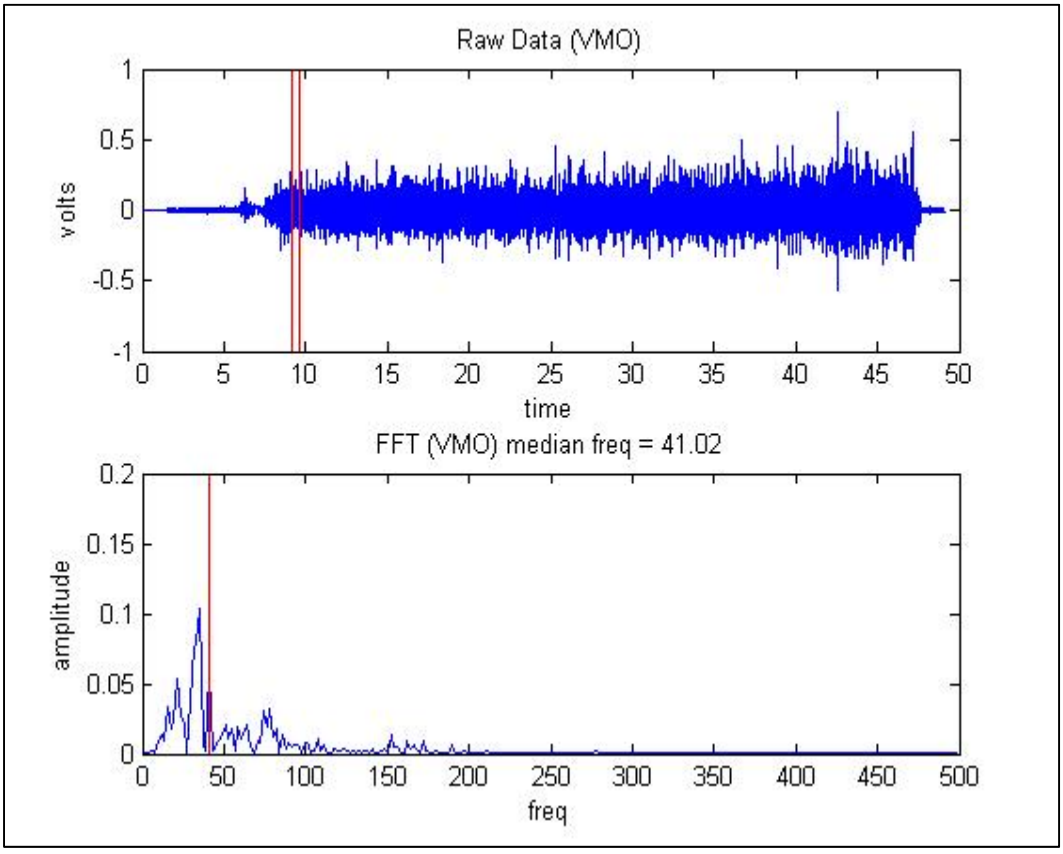
Figure 14B: VMO:VL EMG ratio results for Case Study comparison.



4. Fatigue

Muscle fatigue can be quantified by measuring a shift in sEMG median frequencies (MnF) during a sustained isometric contraction. This shift to lower frequencies can be quantified as an index of fatigue. Figure 15A is a typical response plot during VL fatigue analysis.

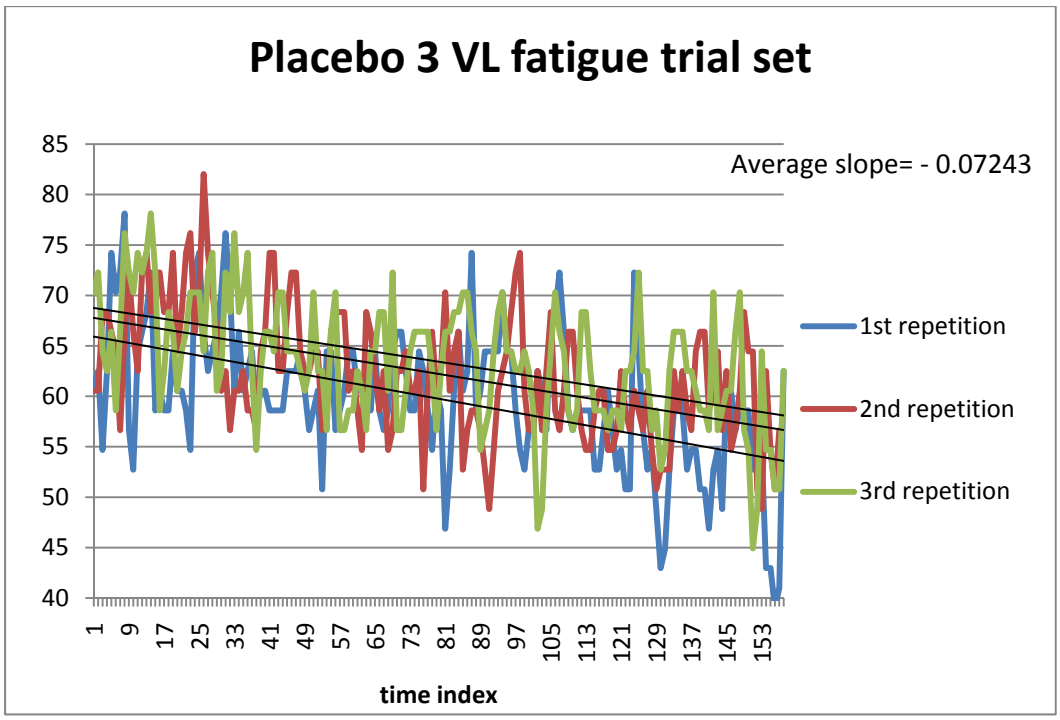
Figure 15A: Typical sEMG data from the VMO muscle during a sustained (40s) isometric contraction.



The top plot illustrates raw sEMG data. The rectangular window (at the 5 second data collection time) denotes the data used in the FFT analysis shown in the bottom plot. The FFT

data was used to compute the MnF which is represented as a vertical red line. The FFT calculation was sequentially executed though the temporal sEMG data stream, providing a series of MnF values. These values were plotted and a liner regression line was fit to the points. An example of this process is illustrated in Figure 15B.

Figure 15B: Typical sEMG median frequency shift for 3 trials of subject Placebo 3.



The average slope was recorded as an "index of fatigue" with a more negative number indicating an increase in fatigue rate. This index is plotted for each session (data collection point) and can be seen in figures 15C and 15D. Note that the Botox™ data includes pilot study results.

Figure 15C: VL Fatigue Differences from baseline. Botox™ data includes pilot study results.

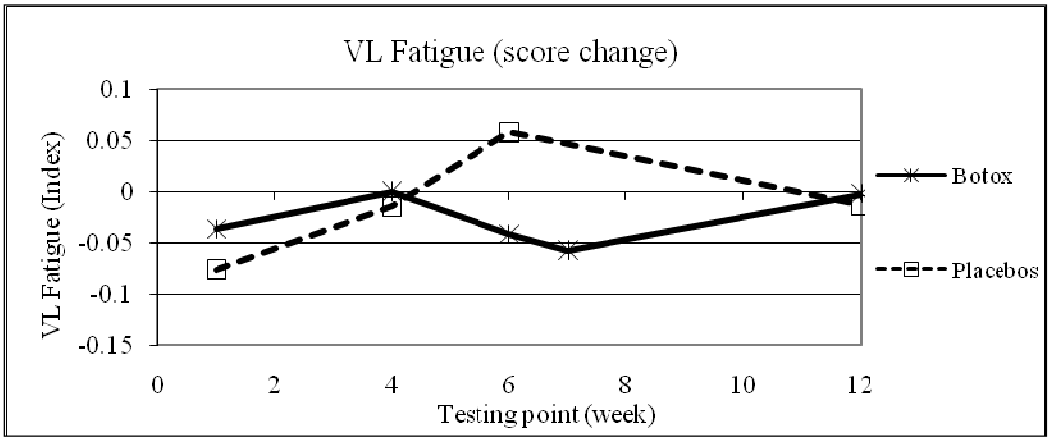
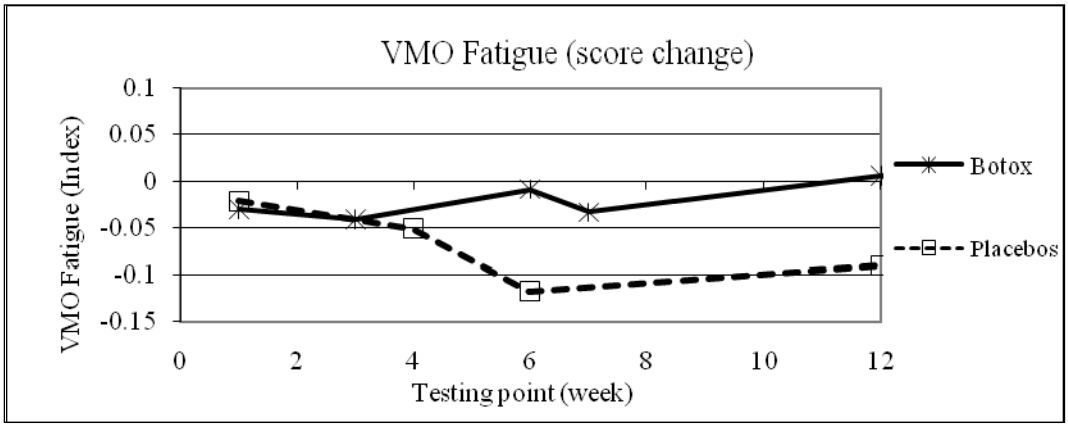


Figure 15D: VMO Fatigue Differences from baseline. Botox™ data includes pilot study results.



The subject who received Botox™ treatment did experience more VL fatigue than subjects who received the placebo. The VMO appeared relatively unchanged in the Botox™ subject, with fatigability increasing in the placebo subjects.

5. Functional Testing

a. Force plate results

Force plates were used to estimate vertical jump height performance. Figure 16A illustrates a force plate similar to the one used in this study. The formula used to determine jump height was based on the amount of time each subject was suspended in the air. The equation used for the jump tests results was:

Jump height (in inches) = $192\ (t/2)^2$

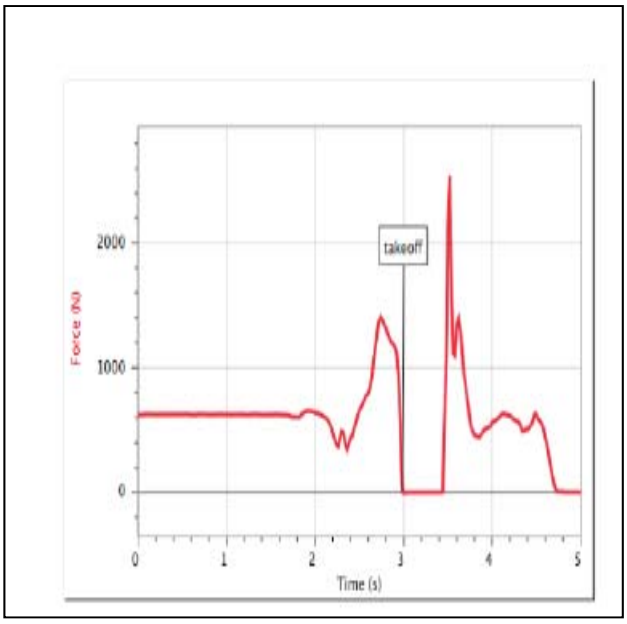
Where: 192 = a constant based on constant acceleration equations

t = time in seconds that the subject is airborne

Longer suspension times represent higher jump height. Averaged flight time during each testing period with their standard deviation is reported in the appendix.

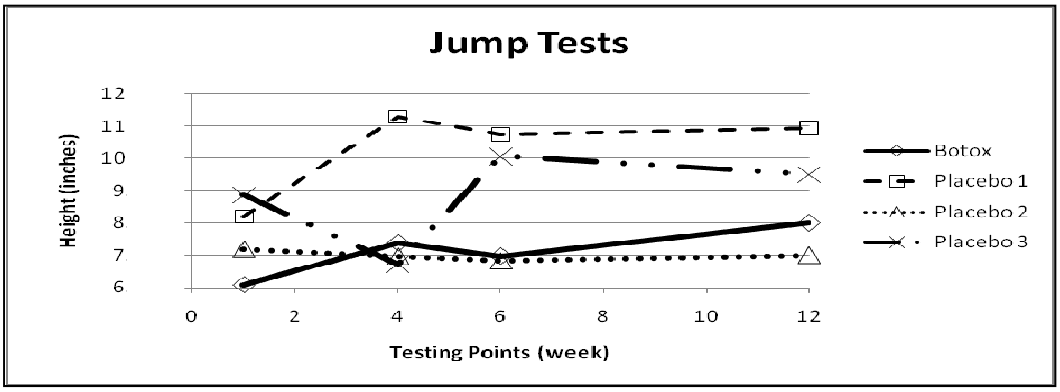
Figure 16: A. An illustration of a typical force plate jump test exercise. B. Illustration of a jump test plot using motion monitor for research after a jump test on a force plate. C. Subject results for force plate jump test trials.

A. 

B. 

In figure 16A, when the subject leaves the force plate, as seen at 3 seconds, there is a loss of foot to force plate contact (the subject becomes airborne). The subject returns to the force plate at the 3.4 second time point. In this example, with the subject airborne for 0.4s equates to a jump height of 7.68 inches. Figure 16C illustrates average jump data from 3 trials at each session. Raw data, averages, and their standard deviations are reported in appendix C.

Figure 16C: Jump height changes.



The Botox™ subject improved in jump height over the course of the study. When comparing baseline to final testing point, the subject who received Botox™ improved in total jump height by +1.91 inches, placebo 1 by +2.73 inches, and placebo 3 by +0.63 inches of a difference in vertical jump height. Placebo 2 had a total jump height difference of -0.19 inches in jump height. Recall that the Botox™ subject and placebo 2 was the same person. The case study data shows that the Botox™ treatment resulted in a jump height 2.10 inches higher than the placebo treatment.

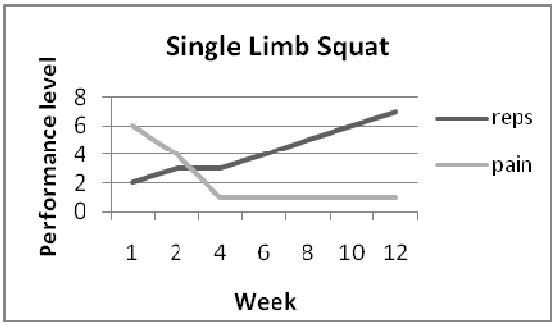
b. Weekly Exercises

Weekly exercises were directed by a physical therapist. The subjects were to follow physical therapists instructions off site. Any issues completing exercises were to be communicated with the physical therapist.

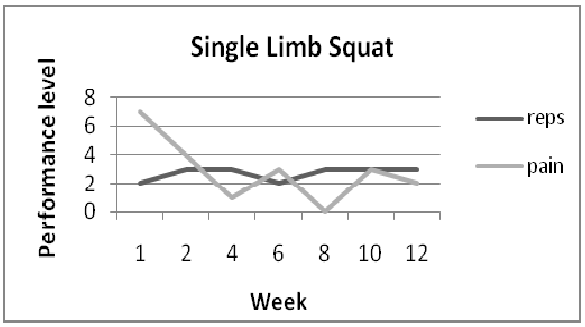
Figures 17A-F illustrate weekly exercise compliance (in repetitions) and pain scores. Repetitions and perceived pain were averaged for a weekly total score. Pain scores were based

on 0, being no pain, and 10, being the most excruciating pain. Subjects were asked to increase the number of exercise repetitions as tolerated.

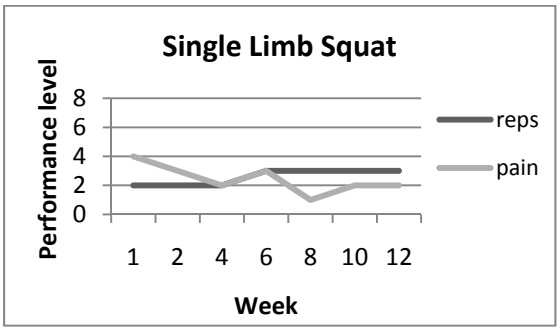
Figure 17A: Weekly exercise result plots for single leg squats illustrating repetition and perceived pain.



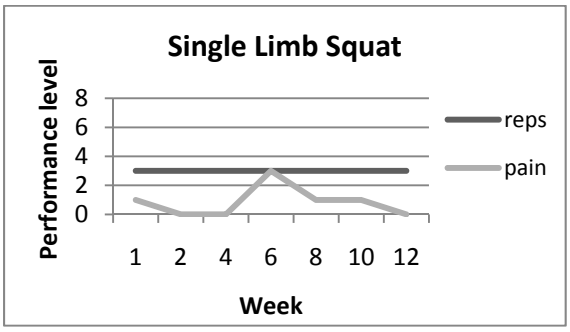
Botox ™ (pain rating decreased 6 to 1)



Placebo 1 (pain rating decreased 7 to 2)



Placebo 2 (pain rating decreased 4 to 2)

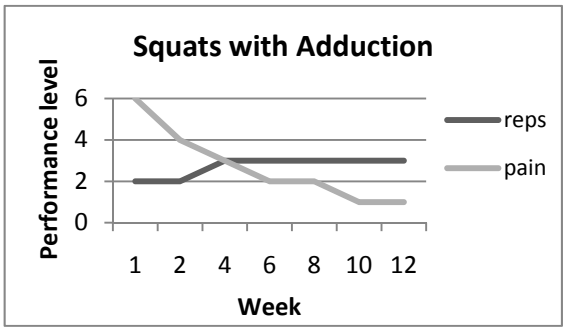


Placebo 3 (pain rating fluctuated)

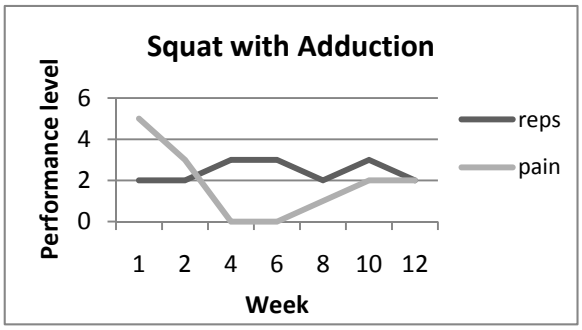
All subjects were able to maintain the prescribed, (3 repetitions as suggested by the physical therapist), repetitions for single limb squats. Performing single limb squat enables each limb to work at their full potential without assistance from the other limb throughout the exercise. The subject receiving Botox™ treatment was able to increase from two to seven repetitions. This was a unique pattern only seen with the Botox™ treatment. Pain also

decreased five points over the course of the study. The placebo subjects showed a fluctuating pattern of perceived pain for this set of exercises.

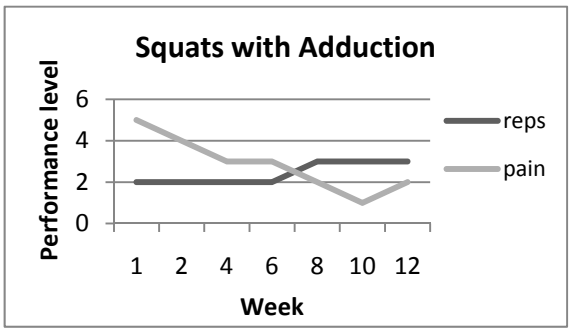
Figure 17B: Weekly exercise graphs for squats with adduction based on repetition and perceived pain.



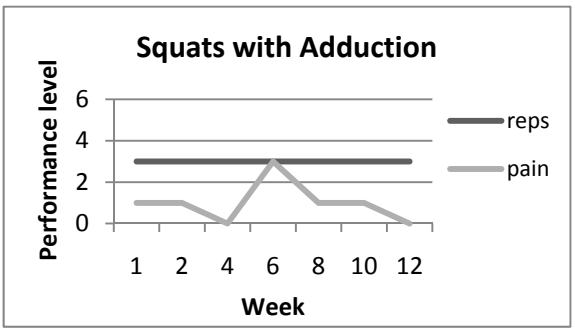
Botox™ (pain rating decreased 6 to 1)



Placebo 1 (pain rating decreased 5 to 2)



Placebo 2 (pain rating decreased 7 to 2)

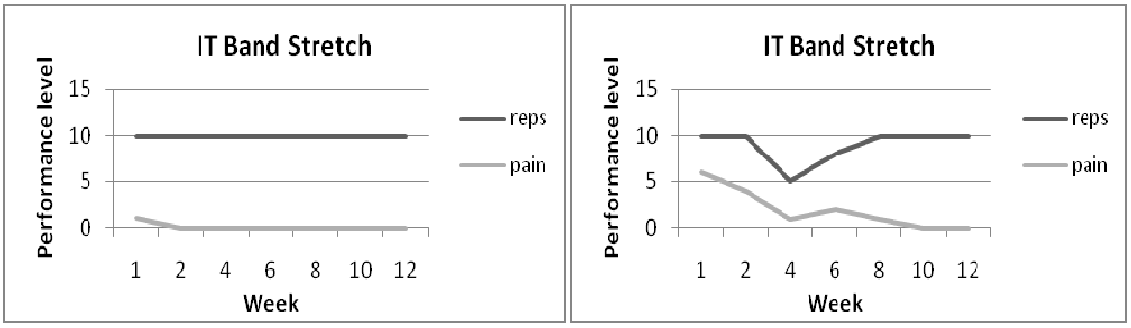


Placebo 3 (pain rating fluctuated)

In figure 17B, all subjects were able to maintain the prescribed repetitions for squats with adduction. The exercise requires the subject to maintain a 90 ° angle at the knee joint with a slight push inwards while performing squats. Three out of the four subjects were able to increase their repetitions. The subject receiving Botox™ treatment in one limb and placebo

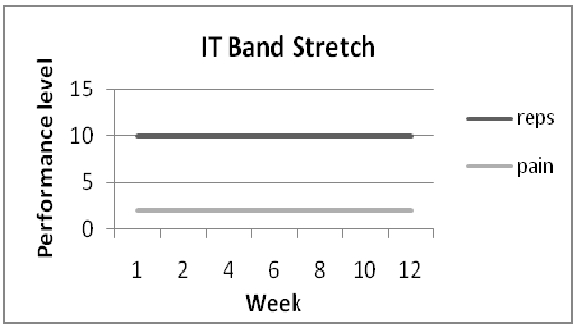
control in the contralateral limb (placebo 2) both decreased pain by five points. A three point decrease was achieved with placebo 1. Placebo 3 had fluctuations in pain rating throughout the course of the study with a one point difference in pain.

Figure 17C: Weekly exercise graphs for IT band stretches based on repetition and perceived pain.

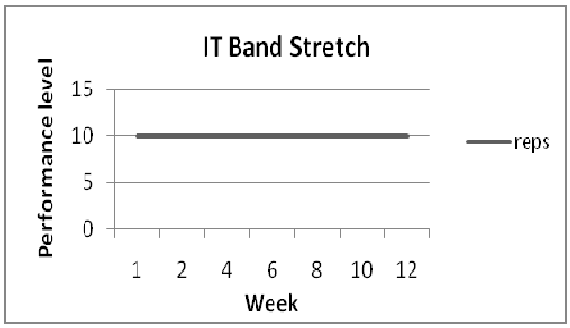


Botox™ (pain rating decreased 1 to 0)

Placebo 1 (pain rating decreased 6 to 0)



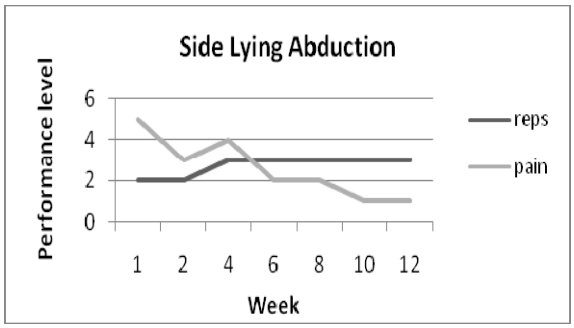
Placebo 2 (pain rating unchanged)



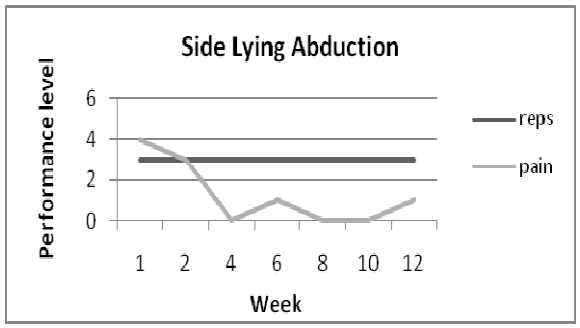
Placebo 3 (pain rating not reported)

In figure 17C, the ten prescribed IT band stretch repetitions were maintained throughout the study. The Botox™ treatment subject and placebo 1 had decreases in their ITB pain. Placebo 2 remained at a three out of ten pain scale, while placebo 3 did not report any pain levels.

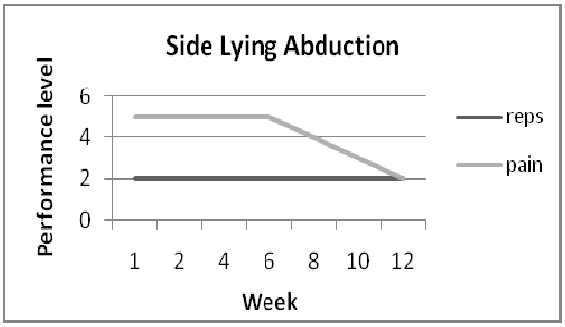
Figure 17D: Weekly exercise graphs for side lying abductions based on repetition and perceived pain.



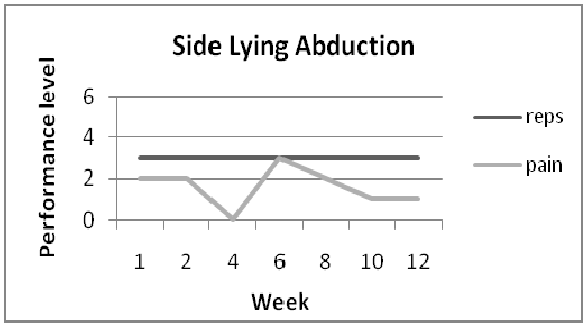
Botox™ (pain rating decreased 5 to 1)



Placebo 1 (pain rating decreased 4 to 1)



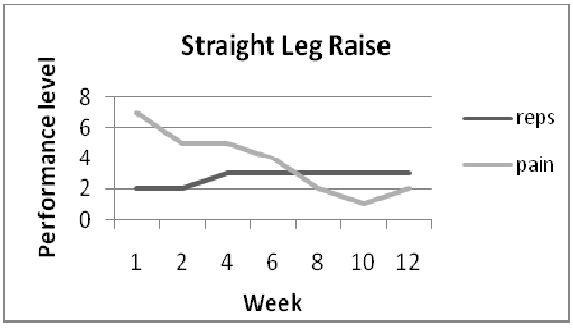
Placebo 2 (pain rating decreased 5 to 2)



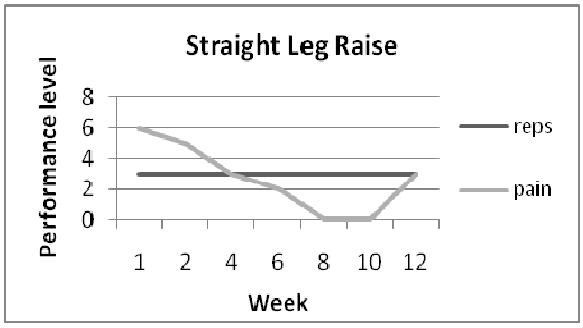
Placebo 3 (pain rating decreased 2 to 1 with fluctuations)

As represented in figure 17D at week 4, the Botox™ treated subject had increased the quantity of repetitions for side lying abduction. All placebo control subjects maintained the original prescribed two repetitions throughout the study. The subject treated with Botox™ also had a 4 point reduction in pain. The placebo controls had a two point average reduction in pain rating for side lying abductions.

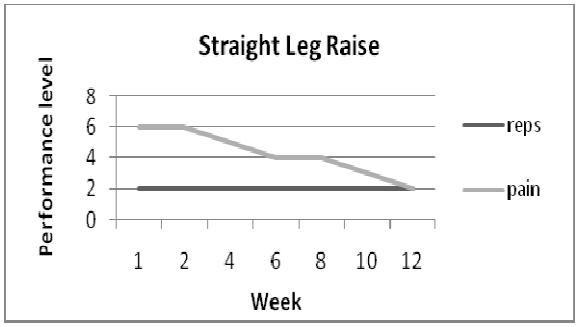
Figure 17E: Weekly exercise graphs for straight leg raise based on repetition and perceived pain.



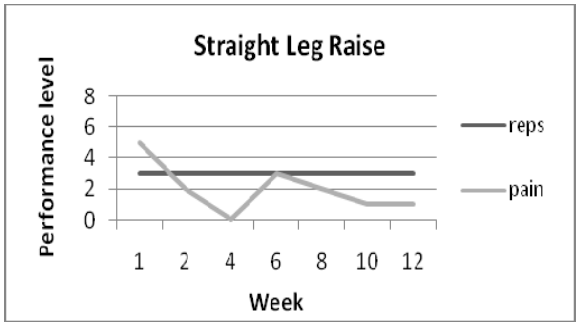
Botox™ (pain rating decreased 7 to 2)



Placebo 1 (pain rating decreased 6 to 3)



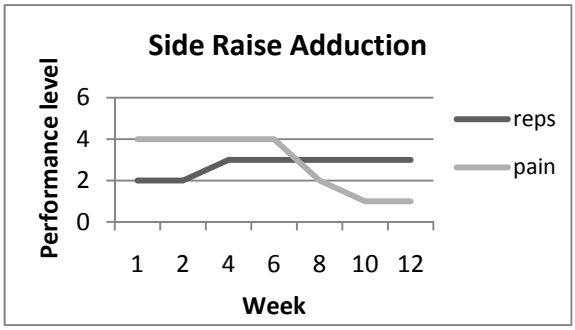
Placebo 2 (pain rating decreased 6 to 2)



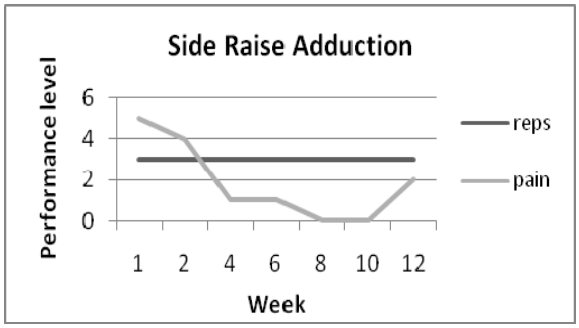
Placebo 3 (pain rating decreased 5 to 1)

In figure 17E, the subject who received the Botox™ treatment increased their straight leg raise repetitions by one at week 4. The other subjects maintained the prescribed two repetitions throughout the study. The subject treated with Botox™ also had a five point reduction in pain. The placebo controls each had a four point reduction in pain.

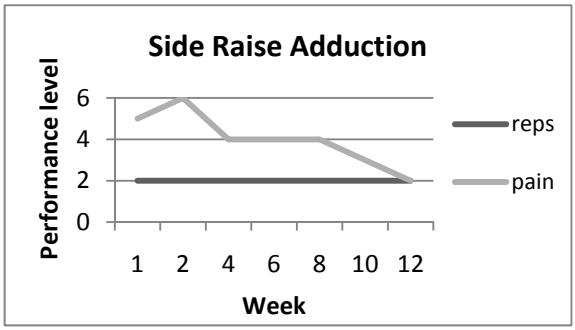
Figure 17F: Weekly exercise graphs for side lying leg adduction based on repetitions and perceived pain.



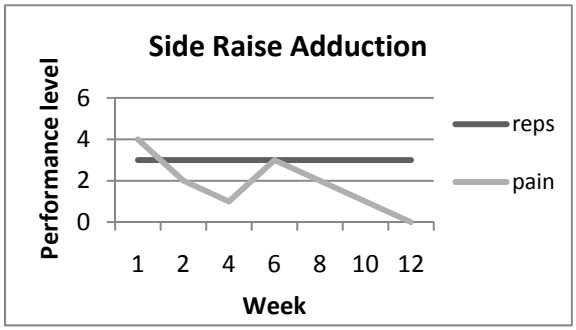
Botox™ (pain rating decreased 4 to 1)



Placebo 1 (pain rating decreased 5 to 2)



Placebo 2 (pain rating decreased 4 to 0)



Placebo 3 (pain rating decreased 4 to 0)

In figure 17F, the subject who received the Botox™ treatment increased the side raise adduction by one repetition at week 4. The other subjects maintained their original prescribed three repetitions throughout the study. Both the Botox™ treated subject and placebo 1 had an overall three point reduction in their pain, while placebos 2 and 3 had a four-point reduction in their pain.

6. Summary of Results

Tables 1 summarize the intra and inter subjective data for the tests that displayed noticeable changes in outcome responses.

Table 1: Summary of Treatment outcomes following Vastus Lateralis Injections

	Botox™	Placebo 1	Placebo 2	Placebo 3
Baseline Pain stair ascending VAS versus post-injection VAS (-10)	6-0 (no pain)	2-1	6-2	5-0
Baseline Pain stair descending VAS versus post-injection VAS (-10)	4-0	2-0	5-3	1-0
Baseline Pain jumping VAS versus post-injection VAS (-10)	5-0 (no pain)	2-2	7-3	7-1
Lower Functional Scale Change	+ 23	+ 8	+ 1	+ 16
Anterior Knee Pain Scale baseline - 12 weeks	75 - 95	57 - 72	73 - 81	69 - 91
Functional Improvement	Greatly improved	No change	Somewhat better	Somewhat better
Injection	Botox™	Placebo	Placebo	Placebo

For the VAS, the treated subject experienced the greatest range of pain loss when ascending and descending stairs. Placebo controls 1 and 3 also reported a final pain level of 0 cm on the VAS for descending stairs, but reported lower baseline ratings. The scale of change was identical to that of the Botox™ treated subject.

The highest possible rating was an 80 for the lower extremity functional scaling (LEFS). The higher valued change indicated the subject was closer to achieving a perfect score. The Botox™ treated subject resulted in the highest value of LEFS change and also experienced the greatest increase in lower functional tasks such as sitting, their typical work and activities.

Placebo control 3 also reported a large improvement in knee function with placebo 2 and placebo 1 (see appendix C for questionnaires) rating the lowest functional improvement.

The highest possible score that could be obtained in the AKP scale was 100. The higher score would indicate no functional knee deficiencies or pain. A 20% improvement in AKP occurred with the subject who received the Botox™ treatment. Placebo 1-3 improved by 15%, 8%, and 22% respectively.

When including the Botox™ pilot data, the three limbs injected were similar in that they were the only individuals to report a "greatly improved" overall study global rating.

Table 2 highlights the objective results.

Table 2: Report of the overall functional-testing summary

	Isokinetic		Isometric		Fatigue	
Subject ID	Work	Power	Torque	VMO/VL	VL	VMO
Botox™	↓	↑	↑	↓	↑	↑
Placebo 1	no change	↑	↑	↑	↓	↓
Placebo 2	↑	↑	↑	↓	↑	↓
Placebo 3	↑	↑	↑	↑	↑	↓
Pilot 1	NA	↑	↑	NA	↑	↑

The subject treated with Botox™ was the only report of decreasing overall work performance. All subjects increased in power and torque. Isometric results indicated both limbs in the case study decreased VMO/VL ratios. The other placebo controls increased in VMO/VL ratio. All subjects, with the exception of placebo 1, increased VL fatigue during testing. Whereas, the VMO an increase in fatigue was demonstrated in the placebo control group and fatigue resistance for the current Botox™ study subject and pilot subjects.

Chapter 4: Discussion

The purpose of this research study is to test the effectiveness of Botox™ in the treatment of muscular imbalances related to PFPS. Without a single standard of measure to categorize subjects suffering from PFPS, this study utilized both subjective and objective tests. Subjective data were collected in the form of questionnaires. These were established tools with proven validity and are often valuable in assessing life-quality issues. Objective data were collected from physical exam and laboratory experimentation. Double blind experimental methods were used to minimize bias in all collected data.

Subjective data

A 10-pt change in Ankle Knee Pain Score (AKPS) reflects a functional change (Crossley, 2004). All subjects had a positive change score in the AKPS. This represents overall improvement (or a decrease in pain) during the course of the study. The largest change was reported by the subject who received the Botox™ injections (+20 pts). The subjects who received Placebo injections also reported positive change, but of much smaller quantity. In fact, the subject label Placebo 2 reported only a one point positive change from baseline. Recall that this is the *case study* subject who received Placebo in one knee and Botox™ in the other knee. Their subjective ratings can therefore be compared and illustrate the magnitude of difference between the two treatments, with the Botox™ treatment producing more positive results.

The Functional Index Questionnaire (FIQ) is an eight-activity multiple-choice rating form where subjects' self-report their ability to complete specific tasks. A score of 16 indicates no difficulty in performing all 8 activities. All subjects demonstrated improvement when measured

using this metric. The subject labeled Placebo 1 had the largest change score and reported perfect score at their final data collection point. This conflicted with that subject's global rating of "slightly better" at the completion of the study. The FIQ data did not illustrate a difference between the Botox™ and Placebo treatments. It has been reported to have poor reliability in some applications (Crossley, 2004). This may be one of them.

The Lower Extremity Functional Scale (LEFS) is a 19-item questionnaire related to activity. These activities range from normal daily activities to recreational exercises. This range is thought to provide a good measure of overall knee function through the assessment of perceived pain. Task scores are converted to a percent composite score. A subject who experiences no difficulty with all 19 tasks would score a 100%. The subject who received the Botox™ injection started the study with a score of 69% and ended with a score of 91%. These was a positive 22.5% overall change in performance. The subjects receiving Placebo injections 1, 2, and 3 showed improvements of only 7.5%, 1%, and 16% respectively with an average percent composite score of 73 ± 2% by the end of the study. The *case study* findings were again very telling, revealing a twenty point overall knee functional improvement for the knee treated with Botox™ as compared to the Placebo as a control.

The Visual Analog Scale (VAS) is a measurement tool to assess knee pain characteristics that cannot be directly measured using other instruments (Gould, 2001). The amount of pain a subject feels is marked on a 10cm line. The left end of that line is labeled "no pain" and the right end is labeled "extreme pain". Subjects were asked to ascend stairs, descend stairs, and jump, marking their VAS scores on a separate scale for each activity. Following patient recording, the distance of the mark from the left edge of the scale was measured and recorded by the examiner. Crossley (2004) reported that a change of two centimeters or more considered significant. All

subjects showed a decrease in pain for each activity through the course of the study. The subjects receiving the Placebo injection had an average decrease of approximately 3cm ascending stairs, 2cm descending stairs, and 3cm jumping. The subject who received the Botox™ injection had a larger change. A 6cm decrease ascending stairs, 4cm descending stairs, and 5cm jumping. Although all subjects demonstrated an overall reduction in pain during all three tasks, the subject receiving the Botox™ treatment had the largest reported reduction (almost double for each activity).

All of these tests reported varying pain reduction and improved knee function for all subjects. Three of these tests differentiated the Botox™ and Placebo subjects. The test that did not differentiate (FIQ) has been previously been reported as unreliable in some applications. The overall improvement of the subjects could be a reflection of increased lower extremity strength resulting from the imposed exercise program; however, the subject who received the Botox™ treatment is the only one who reported both diminished knee pain and a significant overall improvement in knee function. The Ankle Knee Pain Score (AKPS), the Lower Extremity Functional Scale (LEFS), the Visual Analog Scale (VAS) appear to be the most responsive outcome measures for the PFPS population.

Objective data

Isokinetic

One of the objective measures of performance used in this study was isokinetic force production. Isokinetic means constant velocity. In this environment a subject is asked to actively extend their knee against a device (Biodex) that limits terminal (angular) velocity. As the subject pushes harder, resistance is increased using a closed-loop control algorithm. Force

measurements are converted to torque since that force is applied through a known moment arm length. These torque measures are then converted into *work* and *power* for comparison across subjects and trials. A comparison across different angular velocities provides a spectrum of performance characteristics.

Isokinetic *work* was larger at lower angular velocities for all subjects. This is consistent with the physiology of concentric (or shortening) muscle contractions and known force-velocity relationships. At higher velocities, the muscle becomes less capable of producing force since it cannot shorten fast enough. The subject who received the Botox™ injection had a decline in *work* at week 4. This is consistent with the anticipated inhibitory affect of Botox™ on acetylcholine receptors at the muscle fiber motor endplates. This, in fact, was the purpose of the study; to temporarily decrease the force production capability of the lateral muscle group (VL) and allow the medial group (VM) to become relatively stronger. As the effects of the Botox wore off (by week 12), muscle force production returned to appropriate levels. I sokinetic *work* results did not reveal any significant difference between the study groups.

The rate of *work* produced by most muscle is rarely constant. *Power* is often calculated to compensate for rapid time-course changes in *work* and may be more sensitive to performance differences. *Power* is the product of angular torque and angular velocity. For all subjects, more *power* was produced at higher velocities, but the variability of this measure was also higher. This may have been due to subject instruction, limited verbal motivation during the performance of this task, and/or limited practice time prior to the task. Some subjects find it difficult to use an isokinetic dynamometer (Biodex) at higher angular velocities and may need more practice time to become efficient users of this device. At lower angular velocities, data variability was much smaller. The subject treated with Botox™ again showed a marked reduction in *power* at week 4,

but showed signs of recovery by week 6. Isokinetic *power* results did not reveal any significant difference between the study groups. All subjects had an increase in *power* production at all angular velocities when comparing the end of the study to baseline. Since *power* is a more robust measure of performance, this implies an improvement in performance in all subjects. It is important to note that this increase does not signify a change in medial and lateral muscle balance, it just represents an increase in total performance (and that includes force production).

Isometric

Another objective measure often employed to assess muscle performance is isometric force production testing. Isometric means constant length so these data represent force production against a fixed load at a fixed position. Knee positions were varied to get information at different muscle lengths. The data showed higher extension torque production at 30° and 60° of knee flexion when compared to a knee position of 90° of flexion. This was expected since muscle length-tension and patellar moment arm are maximized for performance at 45° of knee flexion. All subjects increased their torque production over time with the highest amount of torque produced during the final week of testing. The Botox™ subject was able to produce more isometric torque than the Placebo subjects at all data collection points. The Botox™ subject also had a slight increase in torque production at week 4. This is contrary to the expected affect of Botox™ and may have been due to a learning effect. In fact, all subjects demonstrated this slight increase at week 4. However, the *case study* comparison showed a difference between the Botox™ and Placebo treatments that disappeared by week 12.

The Botox™ isokinetic and isometric results are consistent with a previous pilot study (Pidcoe, 2006). The only difference is the magnitude of the measurements. The pilot study was

performed on a single male subject who received Botox™ injects to the vastus lateralis muscles of both knees. The current study ended up enrolling only women. There was no effort to normalize data in these studies based on maximum voluntary force production, so the difference in force magnitude is probably due to gender. The important point is the constituency of the results. This provides validity to these results.

Muscle balance (sEMG)

Isometric and isokinetic testing are global measures of muscle performance. They measure force production (or the result of muscle activation) at the distal end of the segment controlled by that muscle group. In our case, the quadriceps muscles are activated to produce and knee extension force (or torque). Muscles produce force as a result of an excitatory neural input. This is an electrical event that results in an excitation-contraction coupling and a subsequent shortening of the muscle fibers. The force produced is positively correlated to the electrical activity in the muscle and can be measured using surface electrodes. Applying electrodes over the medial and lateral muscle groups allows an independent assessment of performance. The collected data is described as surface electromyographic or sEMG.

Medial (VMO) and lateral (VL) muscle sEMG data was collect from each subject while they performed isometric knee extension contractions. The ratio of VMO:VL activation was computed and plotted. A value of 1 would represent a balance between these muscles and equal electrical activity (or equivalent force production). Since the captured electrical activity is a function of electrode placement, care was taken to standardize the methods based on previous published studies. The consistent of the Placebo data suggests that the electrode placement was not an issue.

The VMO:VL ratios demonstrated an increase in VMO activation relative to VL in the subject treated with Botox™. This difference was not evident by week 12 (the end of the study). The Placebo group showed no change in VMO:VL ratio.

These results suggest that the Botox™ injection into VL was successful and decreased the electrical activity of that muscle. Since electrical activity is correlated with force production, it is safe to say that force production of the VL also decreased. This would result in a mechanical change in patellar tracking since both of these muscles attach to the patella and pull it in opposing directions. Coupling these results with the subjective reports of decreased pain and improved function suggests a positive outcome for the Botox™ treatment. These results are consistent with current physical therapy practice where efforts are made to modify patellar tracking to a more medial path in patients suffering from PFPS.

Muscle Fatigue

Another use of sEMG is to assess muscle fatigue. Neuromuscular fatigue is defined as the inability of a muscle to produce force. Muscles differ in fatigue rate secondary to intrinsic and extrinsic properties. These can include muscle fiber type, the general health of the subject, nutrition, previous activity level, and genetics. It is expected that increased workloads will increase fatigue. A work load can increase by increasing the external load or by decreasing the muscle fibers responsible for carrying that load. When the VL muscle was injected with Botox™, it was expected that less fibers would be able to respond to neural excitation. This was evidenced by comparing VMO:VL ratios and the general decrease in torque, work, and power production. It was also expected that this would result in a higher fatigue rate in the VL, since fewer fibers would be doing the same amount of work. The fatigue analysis supports this

expectation. The VL muscle had a higher fatigue rate in the Botox™ subject when compared to the Placebo subjects, while the VMO muscle results appeared unchanged.

Muscles do not add fibers to become stronger. In response to exercise, they do increase the efficiency of each fiber therefore fiber diameter is frequently increased. This increase in muscle "tone" or density may have a mechanical impact on patellar tracking, although the exact ramifications are unknown. It is possible that the reported decrease in pain by the Botox™ subject was due, in part, to a change in patellar tracking resulting from re-balancing the VMO/VL relationship. It is also possible that the decrease in pain reported by all subjects was due, in part, to the overall effect of exercise on increasing muscle "tone".

Functional Testing

Force plate

Subjective VAS data was collected from subjects following a jumping task. These data showed all subjects reported a decrease in perceived pain by the end of the study. Objective data quantifying the jump were also collected. Although there was a variation in the performance of the Placebo group, the important comparison is the *case study* results. These showed that the Botox™ treatment resulted in a jump height 2.10 inches higher than the placebo treatment. It is likely that this improvement was due to both increased muscle force production performance and decreased anterior knee pain. This study can not separate the underlying causes of the improved performance, but can only note that they are related. Higher jumps require larger initiation forces; placing increased compression forces on the patellofemoral joint. A decrease in pain would allow the subject to improve their performance.

Weekly Exercise

As part of the study protocol, subjects were asked to perform a home exercise program (HEP). These exercises were part of a typical physical therapy regiment provided to patients with PFPS. The use of closed chain exercises are an important component of the rehabilitation process. Exercises like partial squats, have been reported by McConnell to prompt the highest activation of the VMO (O'Sullivan, 2005).

During the course of the study, the subjects were asked to record the number of exercises they were able to perform and their perceived pain (with 0 = no pain and 10 = excruciating pain). They were also asked to increase the number of exercise repetitions as tolerated. There progress was monitored by a licensed physical therapist.

The typical pattern for the subject who received Botox™ was an increase in the number of repetitions and a decrease in pain from the beginning to the end of the study. The Placebo subjects often had a similar trend in pain, but were unable to increase the number of repetitions in a prescribed exercise. This has the potential to influence the long-term outcome of the treatment.

Chapter 5: Conclusion

Since 1988, surgical lateral retinaculum release to relieve PFPS has been used with success. Some believe the surgical release can treat both patella pain and some instability issues when used as a treatment for PFPS. However, it is not only an invasive procedure in attempt to release excessive lateral pull on the patella, but surgically, it can also result in potential serious complications (Fox, 1993). Therefore, non-invasive treatments should be considered to treat anterior knee pain.

The subject who received the Botox™ treatment experienced an improvement in functional activities with decreased pain. These findings were consistent with a previous pilot study performed in the same laboratory. The Placebo subjects showed less improvement or experienced no change in symptoms.

As an alternative treatment, Botox™ offers a noninvasive treatment option. The direct results of this study show perceived changes in pain during functional activities and an increase in tolerance to exercise. Indirect results show a change in the balance of medial and lateral muscle groups that may lead to long-term functional improvement. Balance of the knee extensor musculature is critical for optimal patella movement during knee extension (Sanchis-Alfonso, 2006). Restoring the balance of the quadriceps complex should assist in improving normal knee function.

Despite the fact that the research was limited by the small number of participants, Botox™ was found to be safe and effective in treating anterior knee pain.

Future Work

An ideal continuation of this study should include ten subjects with bilateral PFPS. The double blind study should treat one limb with Botox and the contralateral limb with placebo control. To address the study limitations, Botox™ treatment should be offered to those who receive the placebo control as an incentive to participate in the study. This may offset the number of inquiries who only desire the Botox™ treatment option.

Subjective questionnaires could be limited to include only LEFS, VAS, and possibly AKPS. These metrics reported a clear difference between the two treatments. Objective tests should continue to analyze the changes in kinetics and sEMG derivatives.

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Literature Cited

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APPENDIX A

1. Testing Script

Patient: ###
Date: / /
☐ Start time:
☐ End time:
☐ Initiation: Biodex, monitor, and computer on
☐ Computer: Motion monitor on: Joshua
☐motion monitor for research, Botox™, data acquisition, EMG data, view→ toolbars→ new, set-up edit capture parameters- 10 secs record, autosave and add name of file
☐ Click: Capture, record activity
Position, velocity, force, EMG3(VL), EMG4(VM) [box #'s 3 and 4 labeled on the leads box]

☐ Thank patient.
Patient warm-up 5 minutes 50 watts, 50 rpm. Leg positioning should be at 30° at end of pedal stroke.

☐ Explain process and to quickly move to the seat to begin testing while warm.
☐ Seat #__13.0_____
☐ EMG placement- alcohol
leg extended : one handbreadth above patella (EMG3- lateralis)
Four fingers above medial angle of the patella (EMG 4- medialis)

☐Knee alignment
☐Strap in: leg arm number __**. 3048 m 12 on arm**
NOTE: the bottom of the ankle pad is located 1 inch from medial malleolus

☐ISOKINETIC 3 speed, knee, extension/flexion, concentric/concentric
☐ set ROM range _____ (should be close to 100-180 on Biodex screen [10-90 anatomically])

☐ verify 90°, set reference range to 10 and then 90
☐limb weight (stop,enter,start to release leg)
limb weight_____

☐autoscale, 70%, 5 reps, (1 set first for warm-up)
☐make sure speeds are set 1. 180°/s and 180°/s
Do one test run and make sure the strap is tight enough

☐Change sets to three
COUNT STOPS
☐"ask patient to hit button when the red light hits at the end of each set 1.

2. 90°/s 180°/s 2.
☐hit button 3.
3. 45°/s 180°/s
☐hit button
5 reps and 3 sets – 60 sec rest
☐**ISOMETRIC** agonist
☐ verify 90° & set reference to 30° or ☐ set ROM @ 120 ±2 = 30 degree
☐limb weight (stop,enter,start to release leg)
limb weight_____
☐autoscale, 70%, 5 reps, 3 sets
☐hit button after each set
☐60 sec rest COUNT STOPS
☐ set-up, standby, change ROM to 150 = 60 degrees 1.
☐ limb weight _____, autoscale, 70%, 5 reps, 3 sets 2. ☐ set-up, standby, change ROM to 90 degrees 3. ☐ limb weight _____, autoscale, 70%, 5 reps, 3 sets
☐ ESC, ESC, GO to reports, check current date, evaluations, generate reports, F4, max average for ft-lbs, hit F1 to print (see example of print out below). Calculate avg. for 150 (60°) patient average _____

☐hit done on motion monitor, set-up, capture parameters, change period to 50 seconds, change file name

☐**FATIGUE TESTING**
☐ verify 90°, set ROM at 150 (60° position), 40 seconds, 1 rep, at 80%, **place average from isometric testing at (60°)**
☐ limb weight_____
☐Tell patient to aim at the bottom of the line and try to hold it for the 40 seconds
patient doesn't start 2nd set of fatigue until hour glass is off the motion monitor, **Don't** go by stop lights.
☐ Ask patient to hit button after 1 set. COUNT STOPS
☐Repeat, stop
☐Repeat, stop 1.
2.
3.

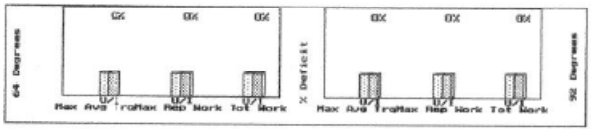
To export: analyze, export, multiple users, user report
C:programfiles:innsport-motion monitor/ user/ Botox/ export

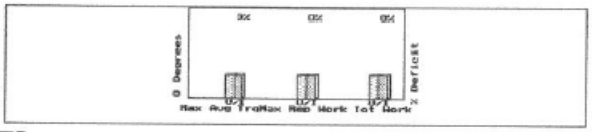
2. Example Printout from the Biodex for Isometric Testing

VCU Dept of Physical Therapy **BIODEX ISOMETRIC BILATERAL EVALUATION**

Name	: Porter	Clinician	:	Joint	: Knee
ID	: 702	Referral	:	Pattern	: Extension/Flexion
Age	: 0	Settings	:	Treatment	:
Sex	: F	Contraction	: Agonist	Involved Side	:
Height (in)	: 67	Test Direction	: Extension	Test Date	: JUN 09, 2007
Weight (lbs)	: 130			Cal. Verification	: OCT 30, 2001 at 08:57

		Position 1 64.0 deg.		Position 2 92.0 deg.		Position 3 0.0 deg.	
		UNI	INV	UNI	INV	UNI	INV
Number of Repetitions	(reps):	3.00	0.0	3.00	0.0	0.0	0.0
Contraction Time	(sec):	5.00	0.0	5.00	0.0	0.0	0.0
Relaxation Time	(sec):	60.0	0.0	60.0	0.0	0.0	0.0
Maximum Average Torque	(ftlbs):	50.0	0.0	66.0	0.0	0.0	0.0
Max. Avg. Torque Rep.	(rep. #):	3.00	0.0	2.00	0.0	0.0	0.0
Coefficient of Variance	(%):	3.03	0.0	2.86	0.0	0.0	0.0
Max. Avg. Torque/Body Weight	(%):	38.5	0.0	50.8	0.0	0.0	0.0
Max. Rep. Work	(ftlbs·s):	151.2	0.0	198.6	0.0	0.0	0.0
Max. Work Rep.	(rep. #):	3.00	0.0	2.00	0.0	0.0	0.0
Max. Rep. Work/Body Weight	(%):	116.3	0.0	152.8	0.0	0.0	0.0
Total Work	(ftlbs·s):	440.9	0.0	583.6	0.0	0.0	0.0
Work First Third	(ftlbs·s):	147.2	0.0	188.1	0.0	0.0	0.0
Work Last Third	(ftlbs·s):	152.2	0.0	196.6	0.0	0.0	0.0
Fatigue	(%):	-3.40	0.0	-4.55	0.0	0.0	0.0
Average Power	(ftlbs):	49.0	0.0	64.8	0.0	0.0	0.0





COMMENTS :

3. Sample of Week 12 Checklist

Week 12 Check List:

Receive forms: LEFS, FIQ, AKPS, VAS*3 Subj # and date – no name	√
Stairs:	
Ascend – VAS	√
Descend – VAS	√
Vertical Jump (three trials):	√
Time	
VAS	
Global rating of satisfaction	√
Biodex testing:	
Isometric, Concentric, Fatigue testing	√
Thank subject	√

4. Example of the End of the study Questionnaire

Subject Number: 703 Date: 1/11/08

Global Rating of Change – Patellofemoral Pain study

Please circle the appropriate response to the following statement:

As a result of participating in this study, my knee* pain is:

Greatly worse
Somewhat worse
Slightly worse
The same
Slightly better
Somewhat better
Greatly better

(* Refers to the knee that was treated as a part of the study)

5. Subject Anthropometric data

Height (inches)	66	63	66	63
Weight (pounds)	128	116	128	105
Moment Arm (meters)	0.3048	0.2794	0.3048	0. 2794

6. Anterior Knee Pain Scale Results

	Botox ™	Placebo 1	Placebo 2	Placebo 3
Session 1	75	57	73	69
Session 2	76	60	79	83
Session 3	77	69	85	73
Session 4	95	72	81	91
Change in Score	+20	+15	+8	+22

7. Functional Index Questionnaire Results. Each question is scored from 0-2, unable to do - no problem (Harrison, 1995).

	Botox ™	Placebo 1	Placebo 2	Placebo 3
Task Session	1,2,3,4	1,2,3,4	1,2,3,4	1,2,3,4
Walking 1 mile	2,2,2,2	1,1,2,2	2,2,2,2	1,1,1,1
Climbing 16 steps	1,2,1,2	1,1,1,2	1,1,1,2	1,2,2,2
Squatting	1,1,1,1	1,1,1,2	1,1,1,1	2,1,1,1
Kneeling	2,1,1,1	1,1,1,2	1,1,1,1	2,1,1,2
Prolonged sitting with knees bent	1,1,1,1	1,1,1,2	1,1,1,1	1,1,1,1
Climbing 32 steps	1,1,1,2	1,1,1,2	1,1,1,2	1,2,2,2
100 meter short run	1,2,2,2	1,1,1,2	2,2,2,2	1,1,2,2
Waking 1 city block	2,2,2,2	1,1,2,2	2,2,2,2	2,2,2,2
Total	11,12,11,13	8,8,10,16	11,11,11,13	11,11,12,13

8. The Lower Extremity Functional Scale Results in percentage.
   A score of 100% represents no difficulty with usual work, hobbies, bathing, walking, putting on shoes, squatting, lifting objects from the floor, performing light activities, getting in/out of car, walking 2 block to a mil, ascending/descending 10 stairs, standing and sitting for 1 hour, running on uneven ground, making sharp turns while running fast, hopping, and rolling out of bed.

	Botox™	Placebo 1	Placebo 2	Placebo 3
Session 1	69	51	80	69
Session 2	87	63	79	71
Session 3	87	65	86	68
Session 4	91	59	81	85

9. Botox Subject: Work and Power results

Botox Subject

WORK					**Power**			
	180°	90°	45°			180°	90°	45°
1	5539	9181	14020		1	4171	3580	2736
4	1042	1562	3005		4	3438	3333	2696
6	2257	4085	5592		6	7365	6221	4073
12	1297	3038	4024		12	4809	5536	3260
Std deviation					**Std deviation**			
1	98	175	436		1	269	155	85
4	178	332	989		4	617	651	945
6	179	373	293		6	585	598	145
12	221	205	589		12	513	449	589

Placebo 1: Work and Power results

Placebo 1

WORK					**Power**			
	180°	90°	45°			180°	90°	45°
1	3834	42	989		1	8823	71	200
4	120	153	191		4	96	60	38
6	103	197	219		6	80	76	42
12	38	50	55		12	13	9	58
Std deviation					**Std deviation**			
1	883	313	436		1	4460	155	85
4	17	6	12		4	13	5	2
6	17	22	28		6	13	9	5
12	5	1	6		12	18	3	21

Placebo 2: Work and Power results

Placebo 2

WORK					**Power**			
	180°	90°	45°			180°	90°	45°
1	2059	3657	5356		1	5465	5498	3829
4	2120	3075	4958		4	6750	5539	3577
6	1920	3733	5891		6	6833	5761	4125
12	2773	5130	6216		12	8983	7505	4282
Std deviation					**Std deviation**			
1	333	337	759		1	1166	543	755
4	512	294	3511		4	1620	581	2394
6	279	526	310		6	1106	843	228
12	420	269	611		12	1546	352	261

Placebo 3: Work and Power results

Placebo 3

WORK					**Power**			
	180°	90°	45°			180°	90°	45°
1	2120	3883	4803		1	7033	6424	3839
4	4297	5108	5250		4	13953	7887	3925
6	4066	5288	5119		6	14682	8397	3902
12	3764	5321	5695		12	14283	8949	4568
Std deviation					**Std deviation**			
1	323	345	380		1	1180	539	305
4	133	378	272		4	561	546	165
6	276	274	826		6	953	388	727
12	95	246	319		12	913	518	382

10. Isometric torque Results in Nm for all study subjects.

Botox™	**30°**	**60°**	**90°**	Placebo 1	**30°**	**60°**	**90°**
1	26	56	59	1	30	55	49
4	57	78	87	4	45	59	57
6	43	73	73	6	40	61	59
12	37	77	75	12	41	64	61
Placebo 2	**30°**	**60°**	**90°**	Placebo 3	**30°**	**60°**	**90°**
1	19	50	60	1	45	51	54
4	51	39	82	4	35	63	63
6	36	75	81	6	41	69	67
12	38	73	84	12	48	77	75

11. EMG ratios of VMO/VL

Botox™	30°	60°	90°	Placebo 1	30°	60°	90°
1	0.91	0.66	0.54	1	0.68	0.69	0.80
4	NA	NA	NA	4	1.00	0.87	0.82
6	0.54	0.52	0.43	6	0.47	0.51	0.45
12	0.55	0.60	0.57	12	0.97	0.88	0.79
Placebo 2	30°	60°	90°	Placebo 3	30°	60°	90°
1	0.44	0.47	0.41	1	0.68	0.61	0.57
4	0.33	0.36	0.34	4	0.50	NA	NA
6	0.37	0.39	0.30	6	0.66	0.70	0.85
12	0.33	0.29	0.36	12	0.76	0.74	0.62

12. Force plate results with flight time during a vertical jump (in seconds).

	Botox™	Placebo 1	Placebo 2	Placebo 3
Week 1	359	413	387	430
Std Dev	3.21	43.6	3.54	31.9
Week 4	392	485	381	374
Std Dev	2.03	22.2	1.41	68.7
Week 6	381	473	377	458
Std Dev	3.06	4.62	3.54	9.54
Week 12	408	477	382	445
Std Dev	21.7	12.5	5.66	6.56

13. Summary of Botox™ Subjects' weekly exercise results

Botox	Single Limb Squat	Squat with adduction	ITB stretch	Side lying Abduction	Straight leg raise	Side raise Adduction
week	reps / pain	reps / pain	reps/ pain	reps / pain	reps / pain	reps / pain
1	2 / 6	2 / 6	10 / 1	2 / 5	2 / 7	2 / 4
2	3 / 4	2 / 4	10 / 0	2 / 3	2 / 5	2 / 4
4	3 / 1	3 / 3	10 / 0	3 / 4	3 / 5	3 / 4
6	4 / 1	3 / 2	10 / 0	3 / 2	3 / 4	3 / 4
8	5 / 1	3 / 2	10 / 0	3 / 2	3 / 2	3 / 2
10	6 / 1	3 / 1	10 / 0	3 / 1	3 / 1	3 / 1
12	7 / 1	3 / 1	10 / 0	3 / 1	3 / 2	3 / 1

Placebo 1	Single Limb Squat	Squat with adduction	ITB stretch	Side lying Abduction	Straight leg raise	Side raise Adduction
week	reps / pain	reps / pain	reps/ pain	reps / pain	reps / pain	reps / pain
1	2 / 7	2 / 5	10 / 7	3 / 4	3 / 6	3 / 5
2	3 / 5	2 / 3	10 / 4	3 / 3	3 / 5	3 / 4
4	3 / 1	3 / 0	10 / 1	3 / 0	3 / 3	3 / 1
6	3 / 3	3 / 0	10 / 2	3 / 1	3 / 2	3 / 1
8	2 / 0	2 / 2	10 / 1	3 / 0	3 / 0	3 / 0
10	3 / 3	3 / 2	10 / 0	3 / 0	3 / 0	3 / 0
12	3 / 2	2 / 2	10 / 0	3 / 1	3 / 2	3 / 2

Weekly exercise report for Placebo 2

Placebo 2	Single Limb Squat	Squat with adduction	ITB stretch	Side lying Abduction	Straight leg raise	Side raise Adduction
week	reps / pain	reps / pain	reps/ pain	reps / pain	reps / pain	reps / pain
1	2 / 4	2 / 5	10 / 2	2 / 5	2 / 6	2 / 5
2	2 / 3	2 / 4	10 / 2	2 / 5	2 /6	2 / 7
4	2/ 2	2 / 3	10 / 2	2 / 5	2 / 5	2 / 4
6	3 / 3	2 / 3	10 / 2	2 / 5	2 / 4	2 / 4
8	3 / 1	3 / 2	10 / 2	2 / 4	2 / 4	2 / 4
10	3 / 2	3 / 1	10 / 2	2 / 3	2 / 3	2 / 3
12	3 / 2	3 / 2	10 / 2	2 / 2	2 / 2	2 / 2

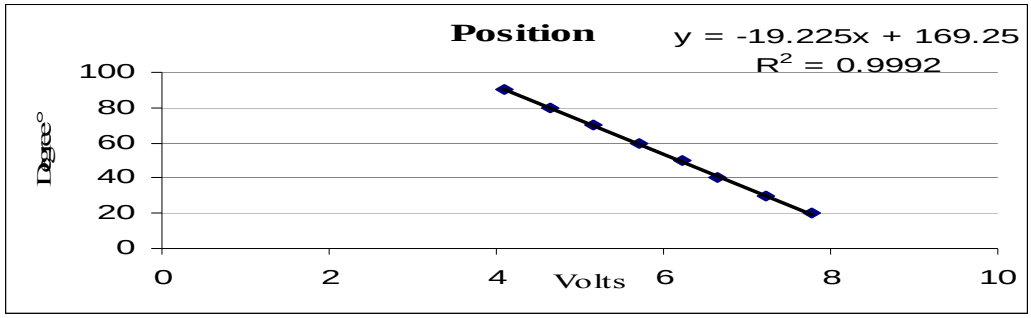
Weekly exercise report for Placebo 3

Placebo 3	Single Limb Squat	Squat with adduction	ITB stretch	Side lying Abduction	Straight leg raise	Side raise Adduction
week	reps / pain	reps / pain	reps/ pain	reps / pain	reps / pain	reps / pain
1	3 / 1	3 / 1	10 / -	3 / 2	3 / 5	3 / 4
2	3 / 0	3 / 1	10 / -	3 / 2	3 /3	3 / 2
4	3 / 0	3 / 0	10 / -	3 / 0	3 / 0	3 / 1
6	3 / 3	3 / 3	10 / -	3 / 3	3 / 3	3 / 3
8	3 / 1	3 / 1	10 / -	3 / 2	3 / 2	3 / 2
10	3 / 1	3 / 1	10 / -	3 / 1	3 / 1	2 / 1
12	3 / 0	3 / 0	10 / -	3 / 1	3 / 1	3 / 0

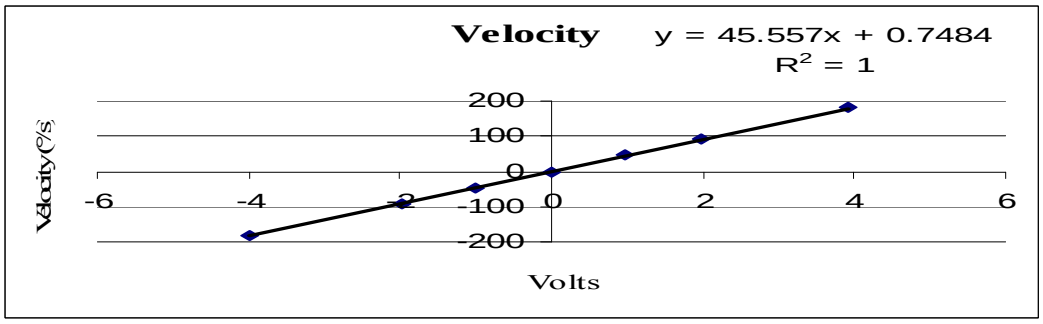
APPENDIX B

CALIBRATION PLOTS

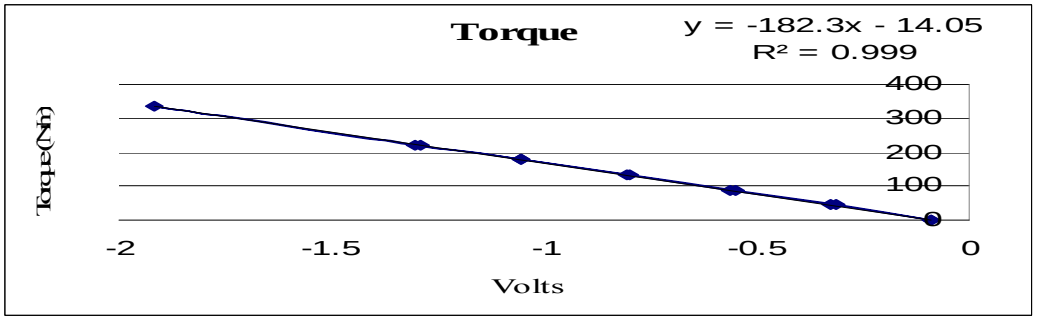
A



B



C



Calibration plots for Biodex used in Matlab programs. Plots A, B, and C are the position, velocity and torque respectively. Calibrations for force, position, and velocity were performed using a simple oscilloscope, and voltmeter. These calibrations convert from a voltage source to a real world degree, degree per second and torque (Nm) during testing sessions.

APPENDIX C

A. **Isokinetic Program**

```
%-------------------------------------------
%  This program is designed to calibrate the
%  pos, vel, and force data
%  PEP 101007
%-------------------------------------------
clear all                          % clear all variables
close all                          % close all windows and files
X=input('Select File to Run: ','s');
Y=load(X);
pos_V=Y(:,2);
vel_V=Y(:,3);
force_V=Y(:,4);
VL_emg=Y(:,5);
VMO_emg=Y(:,6);
file_len=length(pos_V);
RADIAN=3.14/180;

ma=input('Enter moment arm: ');
%ma=.34;

%-------------------------------------------
%  create arrays
%-------------------------------------------
pos_RW=zeros(file_len,1);
vel_RW=zeros(file_len,1);
torque_RW=zeros(file_len,1);
work=zeros(file_len,1);
power=zeros(file_len,1);

segment=zeros(15,1);
%ave_vel=zeros(15,1);
%ave_work=zeros(15,1);
%ave_power=zeros(15,1);
%max_vel=zeros(15,1);
%-------------------------------------------
%  convert data
%-------------------------------------------
for i=1:file_len
   pos_RW(i)=(-19.225*pos_V(i))+169.25;
   vel_RW(i)=(45.557 * vel_V(i))+0.7484;
```

```
   force_RW=-((-182.36*force_V(i))-14.053);  % invert force values
   torque_RW(i)=force_RW * ma;
   work(i)=torque_RW(i)*(pos_RW(i)*RADIAN);
   power(i)=torque_RW(i)*(vel_RW(i)*RADIAN);
end

%-------------------------------------------
%  find concentric segments of data
%-------------------------------------------
k = 1;
loop_len = 5;
flag = 0;
stop = 0;
start=1;

%-------------------------------------------------------------------------
%  Plot results to confirm appropriate selection of data
%-------------------------------------------------------------------------
figure('Name','Torque and EMG Data Window','NumberTitle','off')

% Plot results
subplot(3,1,1)
  hold off
  plot(pos_RW,'b')
    title('Position')
    ylabel('deg')
  hold on
subplot(3,1,2)
  hold off
  plot(torque_RW,'b')
    title('Torque')
    ylabel('lbs-ft?')
  hold on
subplot(3,1,3)
  hold off
  plot(vel_RW,'b')
    title('Velocity')
    ylabel('deg/sec')
  hold on
%-------------------------------------------------------------------------
%  Continue processing data and 1st pass segment bounds.
%-------------------------------------------------------------------------
while (stop == 0)
skip = 0;
for i=start:file_len-loop_len
    if (i == file_len-loop_len)
```

```
      stop = 1;
    end
    flag = 0;
if (skip == 0)
  for j=1:loop_len-1
    if (vel_RW(i+j) > vel_RW(i+j-1) && vel_RW(i+j) > 10)
      flag = flag + 1;
    end
  end
  if (flag == loop_len-1) %found a concentric segment
    for m=i+j:-1:1
      if (vel_RW(m) <= 0 && flag == loop_len-1)
          segment(k) = m;
          %vel_RW(m);
          %flag
          k=k+1;
          flag = -1;
      end
     end
  end
  if (flag == -1) %found beginning concentric, now wait till end to search for next
    for n=segment(k-1)+1:file_len
      if (vel_RW(n) <= 0 && flag == -1)
         segment(k) = n;
         k=k+1;
         flag = 0;
         start=n;
         skip = 1;
      end
      if (n >= file_len) % stop if no end of segment found
         flag = 0;
         k=k-1;
      end
      if (flag == 0)
         break
      end
    end
  end
if (skip == 1)
   break
end
end
end
number = (k-1)/2    %display number of segment
segment (1:number*2,1)  %display segment boundaries
%--------------------------------------------------------------------------
```

```
%  Plot the 1st pass segment bounds.
%------------------------------------------------------------------------
for i=1:number*2
   x = [segment(i) segment(i)]; plot(x,ylim,'r')      % ylim = axis limits
end
%------------------------------------------------------------------------
%  Improve segment bounds estimates. Use the middle 50 points of each
%  velocity segment to determine the base standard deviation. Set a
%  decision threshold at 2x that value. Starting from the middle of a
%  segment and progressing outward in both directions, compute the standard
%  deviation and when it exceeds the threshold, the new segment bounds are
%  stored (replacing the old values).
%------------------------------------------------------------------------
for i=1:2:number*2
   half_len = int16((segment(i+1) - segment(i))/2-25); % center +/- 25 pts
   for j=half_len:-1:1
      start = segment(i)+j-1;
      stop = segment(i+1)-j-1;
      stdev = std(vel_RW(start:stop));
      if (j == half_len)
         threshold = stdev *2;               % threshold at 2 x stdev
      end
      if (stdev > threshold)
         segment(i) = start;                % set new start value
         segment(i+1) = stop;                % set new stop value
         break;
      end
   end
end
%------------------------------------------------------------------------
%  Plot the 2nd pass segment bounds (in green).
%------------------------------------------------------------------------
for i=1:number*2
   x = [segment(i) segment(i)]; plot(x,ylim,'g')      % ylim = axis limits
end
segment (1:number*2,1)  %display segment boundaries
%------------------------------------------------------------------------
%  calculate maximum velocity, average velocity, work and power for
%  concentric knee extension
%------------------------------------------------------------------------
k=1;
for i=1:2:number*2
   ave_work(k) = mean(work(segment(i):segment(i+1)));
   ave_power(k) = mean(power(segment(i):segment(i+1)));
   ave_vel(k) = mean(vel_RW(segment(i):segment(i+1)));
   max_vel(k) = max(vel_RW(segment(i):segment(i+1)));
```

```
%    for j=segment(i):segment(i+1)
%      ave_work(k) = ave_work(k) + work(j);
%      ave_power(k) = ave_power(k) + power(j);
%      ave_vel(k) = ave_vel(k) + vel_RW(j);
%      if (vel_RW(j) > max_vel(k))
%        max_vel(k) = vel_RW(j);
%      end
%    end
%   ave_vel(k) = ave_vel(k) / (segment(i+1)-segment(i));
%   ave_work(k) = ave_work(k) / (segment(i+1)-segment(i));
%   ave_power(k) = ave_power(k) / (segment(i+1)-segment(i));
  k=k+1;
end
t_work = 0;
t_power = 0;
for i=1:number
  t_work = ave_work(i);
  t_power = ave_power(i);
end
t_work = t_work / number;
t_power = t_power / number;
%--------------------------------------------
%  save data
%--------------------------------------------
out=strcat(X,'.cal');
export=[pos_RW vel_RW torque_RW work power];
double(export);
save(out, 'export', '-ascii', '-tabs');
out2=strcat(X,'.ave');
%export=[number t_work t_power];
%double(export);
%save(out2, 'export', '-ascii', '-tabs');
%CHANGE BACK TO COLUMAR DATA OUTPUT -- PEP 021308
export=[max_vel(1:number)'                ave_vel(1:number)'                ave_work(1:number)'
        ave_power(1:number)'];
%export=[max_vel ave_vel ave_work ave_power];
double(export);
save(out2, 'export', '-ascii', '-tabs');
```

B. Isometric Program

```
%-------------------------------------------------------------------------
%  ISOMETRIC.M --
%  This program is designed to calibrate the position, velocity, and torque
%  data. It determines the location of the isometric segment in the data
%  stream and computes the max, min, and average of that segment. It also
```

```
%  computes the RMS EMG for the VMO and VL muscles. All data is restored in
%  text file format.
%  PEP 020408
%--------------------------------------------------------------------------
clear all                               % clear all variables
close all                               % close all windows and files
X=input('Select File to Run: ','s');
Y=load(X);
pos_V=Y(:,2);
vel_V=Y(:,3);
force_V=Y(:,4);
VL_emg=Y(:,5);
VMO_emg=Y(:,6);
file_len=length(pos_V);
RADIAN=3.14/180;
ma=input('Enter moment arm: ');
%ma=.34;
uthresh = input('Enter data start position: ');
if (isempty (uthresh))              % set variable to 1 if no value entered
   uthresh = 1;
end
%--------------------------------------------------------------------------
%  create arrays
%--------------------------------------------------------------------------
pos_RW=zeros(file_len,1);
vel_RW=zeros(file_len,1);
torque_RW=zeros(file_len,1);
work=zeros(file_len,1);
power=zeros(file_len,1);
segment=zeros(15,1);
ave_vel=zeros(15,1);
ave_work=zeros(15,1);
ave_power=zeros(15,1);
max_vel=zeros(15,1);
%--------------------------------------------------------------------------
%  convert data
%--------------------------------------------------------------------------
for i=1:file_len
  pos_RW(i)=(-19.225*pos_V(i))+169.25-180;
  vel_RW(i)=(45.557 * vel_V(i))+0.7484;
  force_RW=-((-182.36*force_V(i))-14.053);  % invert force values
  torque_RW(i)=force_RW * ma;
  work(i)=torque_RW(i)*(pos_RW(i)*RADIAN);
  power(i)=torque_RW(i)*(vel_RW(i)*RADIAN);
end
%--------------------------------------------------------------------------
```

```
%  determine baseline mean and stdv in first 250ms of torque data -- the
%  controlling variable is baseline_size and is initially set to 25
%--------------------------------------------------------------------------
baseline_size = 250;
average = mean(torque_RW(1:baseline_size));
standard_dev = std(torque_RW(1:baseline_size));
%--------------------------------------------------------------------------
%  find isometric segment -- Note: use max torque value as condition to
%  help find end of segment
%--------------------------------------------------------------------------
flag = 0;
file_max = max(torque_RW);
iso_start = 0;
iso_stop = 0;
threshold = average + (4 * standard_dev);
scnt = 500; % start value must exceed threshold for 0.5s (sampled @ 1000Hz)
if (uthresh > 1)
   baseline_size = uthresh; % set start of search to user defined position
end
for i=baseline_size:file_len
   if (torque_RW(i) >= file_max)
      flag = 1;
   end
   if (iso_start == 0 && torque_RW(i) > threshold)
%       iso_start = i;
      cnt = 0;
      for j=i+1:file_len           % look for consistently met threshold
         if (torque_RW(j) > threshold)
            cnt = cnt + 1;
         else
            break;
         end
         if (cnt >= scnt)
            iso_start = i;
            break;
         end
       end
   end
   if (iso_stop == 0 && iso_start > 0 && torque_RW(i) < threshold && flag == 1)
      iso_stop = i;
   end
end
if iso_stop == 0
   iso_stop = file_len;                  % set end to EOF if none found
end
iso_time = (iso_stop - iso_start) / 1000;                  % to be saved
```

```
% Define figure and start plot
figure('Name','Torque and EMG Data Window','NumberTitle','off')
subplot(3,1,1)
  hold off
  plot(torque_RW,'b')
    title('Torque')
    ylabel('Nm')
  hold on
  x = [iso_start iso_start]; plot(x,ylim,'r')   % ylim provides axis limits
  x = [iso_stop iso_stop];   plot(x,ylim,'r')   % ylim provides axis limits
%-------------------------------------------------------------------------
%  compute isometric torque max, min, and average values
%-------------------------------------------------------------------------
max_torque = max(torque_RW(iso_start:iso_stop));            % to be saved
min_torque = min(torque_RW(iso_start:iso_stop));            % to be saved
ave_torque = mean(torque_RW(iso_start:iso_stop));           % to be saved
%-------------------------------------------------------------------------
%  EMG processing
%-------------------------------------------------------------------------
% Determine EMG baseline (for same amount of data used in torque baseline %above
VL_average = mean(VL_emg(1:baseline_size));
VMO_average = mean(VMO_emg(1:baseline_size));
% Subtract baseline from raw EMG data and compute RMS data
for i=1:file_len
   VL_emg_BL = VL_emg(i) - VL_average;
   VMO_emg_BL = VMO_emg(i) - VMO_average
   VL_rms(i) = sqrt(VL_emg_BL * VL_emg_BL);
   VMO_rms(i) = sqrt(VMO_emg_BL * VMO_emg_BL);
end
% Use time constant (TAU) to smooth the data
tau = 250;                    % 25ms equivalent at 1000Hz sampling rate
half_tau = floor(tau / 2);       % round down
for i=half_tau+1:file_len-half_tau
   VL_filt(i) = mean(VL_rms(i-half_tau:i+half_tau));
   VMO_filt(i) = mean(VMO_rms(i-half_tau:i+half_tau));
end
for i=1:half_tau                                % fill in the ends
   VL_filt(i) = VL_filt(half_tau+1);
   VMO_filt(i) = VMO_filt(half_tau+1);
end
for i=file_len-half_tau+1:file_len                    % fill in the ends
   VL_filt(i) = VL_filt(file_len-half_tau);
   VMO_filt(i) = VMO_filt(file_len-half_tau);
end
% Determine average RMS during isometric hold
ave_VL = mean(VL_filt(iso_start:iso_stop));                % to be saved
```

```
ave_VMO = mean(VMO_filt(iso_start:iso_stop));              % to be saved
% Plot results
subplot(3,1,2)
  hold off
  plot(VL_rms,'b')
    title('VL')
    ylabel('v')
  hold on
  plot(VL_filt,'r')
subplot(3,1,3)
  hold off
  plot(VMO_rms,'b')
    title('VMO')
    ylabel('v')
  hold on
  plot(VMO_filt,'r')
%pause;
%---------------------------------------------------------------------------
%  save data (results and processed data)
%---------------------------------------------------------------------------
fid = fopen(strcat(X,'.emg'),'w');
  fprintf(fid,'%s\n',X);
  fprintf(fid,'iso time   = \t%.3f\t sec\n',iso_time);
    fprintf(fid,'start = \t%.3f\t sec\n',iso_start/1000);
    fprintf(fid,'stop = \t%.3f\t sec\n\n',iso_stop/1000);
  fprintf(fid,'ave torque = \t%.3f\t Nm\n',ave_torque);
    fprintf(fid,'max_torque = \t%.3f\t Nm\n',max_torque);
    fprintf(fid,'min_torque = \t%.3f\t Nm\n\n',min_torque);
  fprintf(fid,'ave VL  = \t%.3f\n',ave_VL);
  fprintf(fid,'ave VMO = \t%.3f\n',ave_VMO);
fclose(fid);
out=strcat(X,'.emg_data.xls');
export=[transpose(VL_rms(1:file_len))                                    transpose(VL_filt(1:file_len))
transpose(VMO_rms(1:file_len)) transpose(VMO_filt(1:file_len))];
double(export);
save(out, 'export', '-ascii', '-tabs');
```

C. Fatigue Program

```
%  FATIGUE (botox)
clear all                          % clear all variables
close all                          % close all windows and files
sampling_rate = 1000;              % set to 1000Hz
interval = 1 / sampling_rate;
X=input('Select File to Run: ','s');
Y=load(X);
```

```
pos_V=Y(:,2);
vel_V=Y(:,3);
force_V=Y(:,4);
VL_emg=Y(:,5);
VMO_emg=Y(:,6);
file_len=length(pos_V);
% REMOVE OFFSET FROM DATA
VL_emg = VL_emg - mean(VL_emg);
VMO_emg = VMO_emg - mean(VMO_emg);
% END REMOVE OFFSET
%---------------------------------------------------------------------
%  Find start (t1) and stop (t2) of the usable EMG data based on force
%  data.
%---------------------------------------------------------------------
t1 = 0;
t2 = 0;
threshold = max(force_V) * .5;       % threshold @ 50 percent
for i=1:file_len
   if (t1 == 0 && force_V(i) >= threshold)            % find start
      t1 = i;
   end
   if (t1 > 0 && t2 == 0 && force_V(i) < threshold)  % find stop
      if (i > t1+5000)              % added to reduce false stops
         t2 = i;
      end
   end
end
if (t2 == 0)                        % define stop as EOF if none found
   t2 = file_len;
end
%---------------------------------------------------------------------
%  Plot raw data.
%---------------------------------------------------------------------
close all;
figure('Name','RAW EMG Data Window','NumberTitle','off')
% CREATE TIME ARRAY FOR PLOTTING
cnt=1;
while cnt <= file_len
  xtime(cnt) = (cnt-1)*interval;
  cnt = cnt + 1;
end
%  PLOT RAW DATA
hold off
plot(xtime,VL_emg,'b')
str = sprintf('Raw Data (VL)');
   title(str)
```

```
   xlabel('time')
   ylabel('volts')
hold on
   % overplot start and stop
x = [t1*interval t1*interval]; plot(x,ylim,'r') % ylim = axis limits
x = [t2*interval t2*interval]; plot(x,ylim,'r') % ylim = axis limits
pause(3);
hold off
%--------------------------------------------------------------------------
%  Compute median freq for segments of EMG using and overlap method
%--------------------------------------------------------------------------
fft_len = 512;
count=1;
   start = t1;
   stop = t1+fft_len-1;
while stop < t2
   Raw = VL_emg(start:stop);
% NEW FFT WAY!!!
%array_len = length(Y);
%half_len = int16(array_len / 2);
Y=fft(Raw);
YY=Y.*conj(Y)/length(Y);
f=1000*(0:length(Y)/2)/length(Y);
figure('Name','Data','NumberTitle','off')
subplot(2,1,1)
   plot(xtime,VL_emg,'b')
   str = sprintf('Raw Data (VL)');
      title(str)
      xlabel('time')
      ylabel('volts')
   hold on
   istart = start*interval
   istop = stop*interval
   x = [istart istart]; plot(x,ylim,'r');          % ylim = axis limits
   x = [istop istop]; plot(x,ylim,'r');            % ylim = axis limits
hold off
subplot(2,1,2)
   plot(f(1:int16(length(Y)/2)),YY(1:int16(length(Y)/2)),'b')
   hold on;
% END NEW FFT WAY
% COMPUTE MEDIAN FREQUENCY
cnt = length(Y)/2+1;
sum = 0;
for i=1:cnt
   sum = sum + (1 * YY(i));
end
```

```
half_sum = sum/2;  sum = 0;
i=1;
while sum <= half_sum
   sum = sum + (1 * YY(i));
   median_freq(count) = f(i);
   i = i + 1;
end
count;
median_freq(count);
x = [median_freq(count) median_freq(count)]; plot(x,ylim,'r');       % ylim = axis limits
   str = sprintf('FFT (VL) median freq = %.2f',median_freq(count));
      title(str)
      xlabel('freq')
      ylabel('amplitude')
hold off;
% END COMPUTE MEDIAN FREQUENCY
count=count+1;
pause(2);
close all;
clf;
   j = stop+1 - (fft_len/2);
   start = j;
   stop = j+fft_len-1;
end
%--------------------------------------------------------------------------
%  Plot median frequencies
%--------------------------------------------------------------------------
close all;
figure('Name','Fatigue Analysis','NumberTitle','off')
% CREATE TIME ARRAY FOR PLOTTING
cnt=1;
clear xaxis;
while cnt < count
  xaxis(cnt) = (cnt-1);
  cnt = cnt + 1;
end
%  PLOT RAW DATA
plot(xaxis,median_freq,'b')
str = sprintf('Median Frequency');
   title(str)
   xlabel('count')
   ylabel('Hz')
pause(3);
%--------------------------------------------------------------------------
%  Open a data storage file & store median frequency
%--------------------------------------------------------------------------
```

```
out=strcat(X,'.fat');
export=[median_freq]';
double(export);
save(out, 'export', '-ascii', '-tabs');
close all;
```

APPENDIX D

A. Patellofemoral Pain Study Pre-Study Questionnaire
Name
Age:
Do you have:
Knee pain: Yes No
If yes is your knee pain on the Right or Left
Rate your knee pain on a scale of 0 – 10 (0 no pain, 10 the worst pain you can imagine) _____
Did your pain begin as the result of trauma/injury or did it begin gradually
Have you ever had knee surgery on this knee: Yes No
Has your patellar (kneecap) ever dislocated Yes No

Describe your knee pain in relation to your kneecap ie behind, below, to the inside or outside of the kneecap

Do you have this pain while (put an X next to each one that you answer yes to)
_____ prolonged sitting,
_____ climbing stairs,
_____ squatting,
_____ running,
_____ kneeling,
_____ hopping,
_____ jumping.

How long have you had this knee pain _____

Have you ever had an allergic reaction to Botulinum toxin A (Botox) injection Yes No

Please list all known allergies:

B. Patellofemoral Pain Pre-Study Evaluation

Subject Name _____

Subject Number: _____
Date: _____

Clinical evaluation (first Visit):
Age _____
Height _____
Weight: _____
Pulse: _____
Blood Pressure: _____

Pain on patellar palpation (Yes / No) –

Average pain level on VAS:

Pain onset (insidious vs traumatic) –

Exclusion criteria:
_____ history of knee surgery
_____ history of patellar dislocation
_____ clinical evidence of
____ meniscal lesion,
____ ligamentous instability,
____ traction apophysitis around the patellofemoral complex,
____ patellar tendon pathology,
____ chondral damage,
____ OA
____ spinal referred pain

Inclusion:
Meets Clinical Diagnosis of Patellofemoral Pain Syndrome: **(Yes / No)**

Have you ever had an allergic reaction to a Botulinum Toxin injection:

List allergies:

C. Patellofemoral Pain Prior Perceived pain

Date: _____
Subject Number: _____

No Pain_____ Worst Pain

For the Usual amount of pain you have had today

Indicate on the line where the pain is in relation to the two extremes

D. First preliminary Patellofemoral Pain study visit

Subject Number: _____
Date: _____

Anterior Knee Pain Scale

For each question, circle the latest choice (letter) which corresponds to your knee symptoms

1. Limp
   (a) None (5)
   (b) Slight or periodical (3)
   (c) Constant (0)

2. Support
   (a) Full support without pain (5)
   (b) Painful (3)
   (c) Weight bearing impossible (0)

3. Walking
   (a) Unlimited (5)
   (b) More then 2 km* (3)
   (c) 1-2 km (2)
   (d) Unable (0)

4. Stairs
   (a) No difficulty (10)
   (b) Slight pain when descending (8)
   (c) Pain both when descending and ascending (5)
   (d) Unable (0)

5. Squatting
   (a) No Difficulty (5)
   (b) Repeated squatting painful (4)
   (c) Painful each time (3)
   (d) Possible with partial weight bearing (2)
   (e) Unable (0)

6. Running
   (a) No difficulty (10)
   (b) Pain after more then 2 km* (8)
   (c) Slight pain from start (6)
   (d) Severe pain (3)
   (e) Unable (0)

7. Jumping
   (a) No difficulty (10)
   (b) Slight difficulty (7)
   (c) Constant pain (2)
   (d) Unable (0)

8. Prolonged sitting with knees flexed
   (a) No difficulty (10)
   (b) Pain after exercise (8)
   (c) Constant pain (6)
   (d) Pain forces to extend knees temporarily (4)
   (e) Unable (0)

9. Pain
   (a) None (10)
   (b) Slight and occasional (8)
   (c) Interferes with sleep (6)
   (d) Occasionally severe (4)
   (e) Constant and severe (0)

10. Swelling
   (a) None (10)
   (b) After severe exercise (8)
   (c) After daily activities (6)
   (d) Every evening (4)
   (e) Constant (0)

11. Abnormal kneecap (patella) movements (subluxations)
   (a) None (10)
   (b) Occasionally in Sports activities (6)
   (c) Occasionally in daily activities (4)
   (d) At least one documented dislocation (2)
   (e) More then two dislocations (0)

12. Atrophy of thigh
   (a) None (5)
   (b) Slight (3)
   (c) Severe (0)

13. Flexion deficiency
   (a) None (5)
   (b) Slight (3)
   (c) Severe (0)

* 1 km = 5/8 miles
+ to score, sum the circled responses

Kujala et al: Scoring of Patellofemoral Disorders, J Arthroscopic Rel Surg. 9(2) 159-163, 1993

E. LEFS Form

Subject Number: _____ Date: _____

THE LOWER EXTREMITY FUNCTIONAL SCALE

We are interested in knowing whether you are having any difficulty at all with the activities listed below because of your lower limb problem for which you are currently seeking attention. Please provide an answer for each activity.

Today, do you or would you have any difficulty at all with (circle 1 number on each line):

Activities	Extreme Difficulty or Unable to Perform Activity	Quite a Bit Of Difficulty	Moderate Difficulty	A Little Bit of Difficulty	No Difficulty
a. Any of your usual work, housework, or school activities.	0	1	2	3	4
b. Your usual hobbies, recreational or sporting activities.	0	1	2	3	4
c. Getting into or out of the bath.	0	1	2	3	4
d. Walking between rooms.	0	1	2	3	4
e. Putting on your shoes or socks.	0	1	2	3	4
f. Squatting.	0	1	2	3	4
g. Lifting an object like a bag of groceries from the floor.	0	1	2	3	4
h. Performing light activities around your home.	0	1	2	3	4
i. Performing heavy activities around your home.	0	1	2	3	4
j. Getting into or out of a car.	0	1	2	3	4
k. Walking 2 blocks.	0	1	2	3	4
l. Walking a mile.	0	1	2	3	4
m. Going up or down 10 stairs (about 1 flight of stairs)	0	1	2	3	4
n. Standing for 1 hour.	0	1	2	3	4
o. Sitting for 1 hour.	0	1	2	3	4
p. Running on even ground.	0	1	2	3	4
q. Making sharp turns while running fast.	0	1	2	3	4
r. Hopping.	0	1	2	3	4
s. Rolling over in bed.	0	1	2	3	4
Column Totals:					

SCORE: / 80

Minimum Level of Detectable Change (90% Confidence): 9 points

Binkley, J., Stratford, P., Lott, S., et al. The Lower Extremity Functional Scale: Scale development, measurement properties, and clinical application, Phys Ther. 79:4371-83, 1999.

F. Patellofemoral Pain VAS for ascending, descending, and jumping

Date: _____

Subject Number: _____

For the amount of pain you had ascending stairs
Indicate on the line where the pain is in relation to the two extremes

No Pain _____ Worst Pain

For the amount of pain you had descending stairs
Indicate on the line where the pain is in relation to the two extremes

No Pain _____ Worst Pain

For the amount of pain you had while jumping
Indicate on the line where the pain is in relation to the two extremes

No Pain _____ Worst Pain

Jumping Time suspended:

_____

G. Patellofemoral Pain VAS for great and usual Pain

Date: _____

Subject Number: _____

For the **Greatest** amount of pain you have had today
Indicate on the line where the pain is in relation to the two extremes

No Pain _____ Worst Pain

For the **Usual** amount of pain you have had today
Indicate on the line where the pain is in relation to the two extremes

No Pain _____ Worst Pain

After Completion place in envelope and return at your next study appointment

VITA

Laura Maple was born and raised in Virginia in January 1980. She is a United States citizen who has attending Louisburg College in North Carolina and Virginia Commonwealth University. She earned her bachelor's of Science at VCU in Chemistry while being on the Dean's List and a member of the National Chemical Society. She was awarded as the recipient of the Ingraham Scholarship. Since graduating from undergraduate school Laura has published in the Journal of American Society for Mass Spectrometry, "Evaluation of Sample Preparation Techniques for mass measurements of PCR products using ESI-FT- ICR Mass Spectrometry and in_Drug Monitoring and Toxicology, for Development and validation of ELISA for Herceptin detection in human serum.